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OBSTETRICAL  
AND  
GYNECOLOGICAL  
SURVEY

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# OBSTETRICAL AND GYNECOLOGICAL SURVEY

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VOLUME 1

OCTOBER 1946

NUMBER 5

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## FOREWORD

In presenting this, the initial number of the Obstetrical and Gynecological Survey, the Editors feel that some explanation is proper as to the planned purpose and scope of the publication. It would hardly seem necessary to elaborate upon the advantages of making available to busy practitioners all the important literature of the world in abstract form. This, however, will be true only if the abstracts are well selected and properly prepared. For example, they should really represent the essence of the original publications, and they should be sufficiently full so that in most instances they will suffice to give the average reader all the information he wishes, without the necessity of going back to the original paper. Too short and too perfunctory abstracts are of little or no value except as references, and the reader is too often driven to the irritating necessity of digging out the original publications. The Editors have assumed the responsibility of maintaining these high standards for the abstracts appearing in the Survey, and they will do their best along these lines.

In this country there is only one journal devoted exclusively to the field of obstetrics and gynecology, the excellent American Journal of Obstetrics and Gynecology. In addition to this, a number of other periodicals include obstetrics and gynecology within their stated scope, though all too often in only a minor and submerged fashion. Finally, papers on our specialty, sometimes quite valuable, not infrequently appear in our national weekly, the Journal of the American Medical Association, and also in periodicals of state or regional scope as well as in journals devoted to other special fields, such as endocrinology. Even in the national field, therefore, it is difficult for one to keep abreast of the literature without some such help as the Survey affords.

Even more important, however, is the fact that the literature of the rest of the world is to all intents and purposes beyond the reach of most readers, not only because of the unavailability of the original publications, but because most of them are in foreign languages. The war has of course almost put a stop to the free flow of these foreign publications, but before long they will again become available, and will form a larger and larger part of the material reviewed in the Survey.

It is planned to make the Survey a truly international publication, and this is indicated by the fact that our Editorial Board includes distinguished leaders in the field of obstetrics and gynecology in quite a number of countries, with others to be added from other nations, such as Russia and France, just as soon as international and national conditions justify this. In this cooperative international sense, the Survey will perhaps differ from the former German publication, the *Berichte über die gesamte Gynäkologie und Geburtshilfe*, but in other respects, especially in the international coverage of the literary front in obstetrics and gynecology, we hope to do as complete and valuable a job as was done by the *Berichte*.

The editorial comments made upon many of the abstracts appearing in the

Survey are appended, not to give the Editors an opportunity to air their own opinions, but rather to permit of evaluation of the abstracted papers in the light of accepted opinion and practices. Since many papers deal with unsettled or perhaps controversial subjects, it is quite certain that the comments of the Editors will not always meet with universal approval, but perhaps this very human difference of opinion may add some zest to the publication as a whole.

Last but not least, it is planned to publish from time to time comprehensive reviews of subjects of current interest in the field of obstetrics and gynecology, contributed by well qualified authors, preferably those identified with the subjects to be presented. A review of this type is published in this issue, and others will appear at intervals to be determined as the Survey expands. In the preparation of these comprehensive reviews, it is hoped that our foreign colleagues will later play an important part.

This, then, is a brief outline of what is planned for the immediate future, although still other more distant ambitions are being nurtured for the years to come. While there are abstract journals of various sorts and in various fields, it should be made plain that the Survey is an entirely new project, with no connection whatsoever with any other periodical in the field. An enormous initial asset is the fact that it is published by a well-known and long-established publishing firm, the Williams and Wilkins Co. Like the Editors, the publishers feel that the Survey will supply a genuine need, and that it has unlimited possibilities for the future. Its sponsorship by such a fine publishing house assures the continuity and financial security of the new publication. The Editors on their part pledge themselves to the highest possible scientific and editorial standards. They will do their best to make the Survey a credit to our specialty.

—THE EDITORS.

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# Obstetrics

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## DIABETES MELLITUS AND PREGNANCY

### A REVIEW

By NICHOLSON J. EASTMAN<sup>1</sup>

Baltimore, Md.

#### THE PRE-INSULIN ERA

Prior to the advent of insulin in 1921 the great majority of diabetic women were sterile. In one of the earliest papers on the subject, published by J. Matthews Duncan in 1882, the author writes: "The rarity (of pregnancy complicating diabetes) is attested not only by its having no historical place in literature, but by the actual experience of accoucheurs and of hospitals. We are constantly seeing nephritic and febrile and other complications, but this complication very rarely." He was able to collect from the literature but thirteen cases and added three of his own. Griesinger, a German clinician of the same period observed two pregnancies among fifty-three diabetic women, while Frerichs encountered but one pregnancy in 104 diabetics of the female sex. The studies of Lecorché (1885) and von Noorden (1909) showed somewhat higher pregnancy rates, the former reporting seven gestations in 114 diabetic women (6 per cent) and the latter twenty-three pregnancies among 427 diabetic women of the child-bearing age (5 per cent). At the London Hospital during the years 1893 to 1922, 190 married diabetic women up to the age of forty-six years were admitted and of these 4, or 2 per cent, were pregnant; from 1923 to 1931, 177 were admitted of whom 27, or 15 per cent, were pregnant, a seven-fold increase in the incidence of pregnancy (Skipper). In 1909 J. Whitridge Williams, after thirteen years as head of the Obstetrical Service of the Johns Hopkins Hospital and despite a large consulting practice, had himself encountered but one case of diabetes complicated by pregnancy. During the past ten years in that same hospital, among 227 married diabetic women between the ages of fifteen and forty-five who were admitted, sixty-five, or 28.6 per cent, were pregnant. By coincidence this number of pregnant diabetics seen at the Johns Hopkins Hospital during the past decade, namely sixty-five, happens to be the precise number which Dr. Williams was able to collect from the entire world's literature in 1909.

The underlying cause of the lack of fertility in diabetes during the pre-insulin era was probably due to a number of factors most of which are poorly understood. Structural changes have been observed in the reproductive organs of diabetics by a number of authors. Thus, Parisot has described the disappearance of

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Graafian follicles in diabetes. Atrophy of the uterus has been demonstrated by Graefe; while Priscilla White and her associates have observed lack of development of the genital tract at autopsy in four young patients whose diabetes was of long standing. Amenorrhea was not uncommon in diabetes during the pre-insulin period, Parisot placing the incidence as high as 50 per cent. Other authors cite much lower figures and all agree that sometimes even the severest diabetics of that era menstruated regularly. Skipper has observed a diabetic in whom menstruation, absent for ten years, returned when the patient was given insulin. Fitz and Murphy, and B. D. Bowen have each reported a case in which amenorrhea of two years' duration was followed, after treatment with insulin, by menstruation, and later by pregnancy. In experimental diabetes, according to Hoffmann, the testicles undergo marked degenerative changes but ovarian alterations are much less pronounced. Contrariwise, the castration experiments of the same author resulted in hypertrophy of the islands of Langerhans. This experimental work, as well as the clinical observations cited, substantiates the viewpoint that the pancreas is an integral portion of a complex endocrine system and that any marked deviation from normal function on the part of any component affects the others. On this basis the most likely cause of the infertility of diabetic women in the pre-insulin era was hyper- or hypofunction of the "master-clock" of the generative tract, the anterior pituitary gland. Actual histological proof that this gland is regularly altered in diabetics, however, is lacking since the many studies on the subject either show no changes in the gland, or are so conflicting as to raise some question about the validity of the findings. In addition to endocrine imbalance, nutritional deficiencies must have entered appreciably into the infertility of diabetics before the insulin era since the restricted diets necessary probably entailed dire, if inadvertent, reduction in food elements essential for reproduction.

When diabetic women did occasionally become pregnant in the pre-insulin era, some 25 per cent of the mothers and about 50 per cent of the infants died. The pitiful state of pregnant diabetics in those days is graphically portrayed by Mathews Duncan in his detailed case histories: "the mawkish sweetness of the breath," "the sticky amniotic fluid," the intense thirst and tremendous polyuria recur in case after case. In one of his patients "the thirst became 'frightful' and being refused water by the nurse, she crept on her hands and knees to the water bottle." In the sixteen cases reported by Duncan (three his own, and thirteen from the literature), four women died very shortly after delivery, that is, one-quarter. In Williams' sixty-six cases, there was an immediate maternal mortality of 27 per cent. In a noteworthy German study of that period, published by Offergeld in 1908, the maternal loss was 30 per cent. Most of these women died with the characteristic picture of acidosis and coma shortly after delivery. The infant mortality in the three series mentioned was 47, 41 and 62 per cent, respectively.

*The experience of the pre-insulin era, as surveyed above, is not merely of historical interest but is of great clinical importance, because it shows that untreated diabetes and pregnancy are basically incompatible. On the one hand, the disease if un-*

controlled so disrupts the reproductive mechanism as to make successful child-bearing almost impossible. On the other hand, untreated diabetes is aggravated by pregnancy to a degree which is often fatal. *This mutual incompatibility between neglected diabetes mellitus and pregnancy demands emphasis because only in so far as the disease process can be meticulously controlled and the associated metabolic disturbances curbed, may its baneful effects on the child-bearing woman and her infant be forestalled.*

#### INCIDENCE

As mentioned above, sixty-five cases of diabetes in pregnant women have been observed at the Johns Hopkins Hospital during the past decade. Since, in the same period, 18,225 deliveries took place in the institution, the incidence of diabetes in these child-bearing women was 1 in 282. In the population at large the incidence is doubtless less than this because some of the diabetic gravidæ in the above series were referred to the clinic because of the disease. On the basis of this and other series, however, it would appear that the practitioner may expect to encounter a case of diabetes complicated by gestation about once in every three or four hundred pregnancies.

It is well known that the incidence of diabetes increases sharply with age and that the maximum susceptibility to the development of the disease in women is not reached until the mid fifties. Thus, Joslin's adaptation of the statistics of the National Health Survey covering 2,500,000 persons, shows that in females between 15 and 24, the frequency of diabetes is 1:1700; between 25 and 34, 1:900; between 35 and 44, 1:300; between 45 and 54, 1:125; between 55 and 64, 1:50 and in women 65 and over, 1:45. Not only is diabetes much more common after the menopause, but its frequency in women between 35 and 44, is three times that seen in women between 25 and 34, and five times the incidence encountered in females between 15 and 24. These figures not only explain the relative infrequency of diabetes in pregnancy, but call to our attention an important clinical fact: *when diabetes is encountered in pregnancy, the chances are greatly in favor of its being met in older women in whom, as is well known, various other complications are more frequent, particularly hypertension.* The age factor, hence, will often itself contribute a count against diabetic gravidæ.

#### DIAGNOSIS

The presence of sugar in the urine of a pregnant woman may indicate one of three conditions or any combination of them: (1) lactosuria; (2) renal glycosuria; (3) diabetes.

*Lactosuria.* The occasional occurrence of lactosuria in late pregnancy, and more particularly in the puerperium, is well known and quite understandable. From a practical point of view the sole question is how often is it encountered and in what degree; in other words, how frequently is it a potential source of error in the diagnosis and management of diabetes in child-bearing women?

It is common knowledge that infinitesimal amounts of reducing substances are present in the urines of all persons. Long ago Folin and Berglund demon-

strated that these reducing substances are polysaccharide sugars from the food and other bodies, non-carbohydrate in character, which the organism is unable to utilize and so excretes by way of the kidneys. In most normal urines figures for these reducing bodies lie between 20 and 70 mg. per 100 cc. of urine and they rarely exceed 100 mg. Except in pregnancy these "normal" reducing bodies are not affected by yeast and therefore, like lactose, are non-fermentable reducing bodies indistinguishable from lactose except by very especial techniques. These bodies are not detectable by the commonly used Benedict qualitative test since that reagent only begins to yield a faint positive reaction (the slightest possible change to green) between 100 and 150 mg. of sugar or its equivalent. Making use of very delicate methods several authors have shown that in pregnancy an appreciable portion of this "microscopic" sugar is lactose and point out that lactosuria in minute degree is the rule during gestation. This is understandable since mammary activity is progressive throughout pregnancy. However, these infinitesimal amounts of lactose are of no concern clinically since they do not give a positive Benedict reaction and accordingly would never give rise to a false diagnosis of glycosuria.

If attention be limited then to lactosuria of 100 mg. per cent or more, enough to give at least a faint Benedict reaction, the literature on the incidence of the condition in child-bearing women may be summarized as follows: (1) Except for the last six weeks, lactosuria in pregnancy is not common being seen in but 1 or 2 per cent of gravidæ. Snoeck's figure for this general period is 1 per cent. (2) During the last six weeks its frequency increases, Snoeck finding an incidence of 7 per cent. In a careful quantitative study of fifty pregnant women (stage not stated) by Richardson and Bitter, four patients or 8 per cent showed lactosuria in excess of 100 mg. per cent. As term approaches the incidence of the condition rises steeply and on the day before delivery urinary lactose is demonstrable in a third or more cases. Thus, Rowe, Gallivan and Mathews found it present in nineteen of fifty cases, or 38 per cent, on the day before delivery. In a detailed study of lactose metabolism in women, carried out in 1928 by O. Watkins, daily figures are given for lactose excretion in four representative cases during the last ten to fifty days of pregnancy. These were, on the day before delivery, 63, 842, 164 and 133 mg. per cent, respectively. In the second of these cases, certainly, large amounts of lactose were being excreted. In all the patients studied by her the lactose excretion began to rise on the third to sixth day before delivery and reached its maximum on the day when labor set in. On the day after delivery there was a sharp drop to a level which in most cases was lower than that shown at any other time, either before or after delivery. (3) Lactosuria is most frequent and most marked in the puerperium. In Richardson and Bitter's study of fifty women on the twelfth day postpartum, twenty or 40 per cent showed a concentration of lactose in the urine of more than 100 mg. per cent; in one case the figure was 406; and the average for the entire fifty women was 99 mg. per cent. If daily lactose determinations are carried out, as was done in Watkins' study, all puerperal women will show, on one day or another, urinary lactose well in excess of 100 mg. per cent. Rowe, Gallivan and Mathews were

able to demonstrate its presence in 100 per cent of specimens obtained on the third and fourth days postpartum, in 92 per cent on the tenth day and in 82 per cent on the fourteenth day. The excretion of this sugar, moreover, seems to persist in a high percentage of cases as long as lactation continues since these same authors found it in 80 per cent of nursing mothers six months after delivery. Not infrequently; particularly early in the puerperium, the urine contains large amounts of lactose and in several such cases of Watkins the concentration ranged between 1000 and 1390 mg. per cent, that is, 1 per cent and above.

The main deductions of clinical importance which issue from the above survey are as follows: (1) Many women in the early days of the puerperium excrete lactose in concentrations of 1 per cent and higher. This may well mean 10 gm. and more of this sugar in a twenty-four hour specimen. Diabetes in no way alters this excretion of lactose with the result that in puerperal diabetics the two sugars, glucose and lactose, often appear in the urine together. Obviously, unless the physician knows accurately, by means of fermentation tests, how much of any urinary sugar at this time is glucose and how much is lactose, he will be completely confounded in his evaluation of the diabetic status. (2) As full term approaches, especially, during the last few days, it becomes more and more likely that any sugar found in the urine is lactose. (3) Prior to the last six weeks of pregnancy lactosuria of sufficient degree to give a positive Benedict reaction is uncommon, but since it does occur occasionally it should be routine to perform fermentation tests on all urine specimens from pregnant women which show sugar; at this stage of gestation, however, the chances are against the sugar being lactose, as will be brought out in the following paragraphs.

*Renal glycosuria.* Abundant evidence attests the fact that pregnant women show an increased tendency to excrete glucose in the urine. This evidence is several-fold: (1) the relatively high frequency with which glycosuria is encountered in pregnant women, as reported in many series of cases; (2) the fact that the majority of pregnant women, following the ingestion of 100 grams of glucose will exhibit glycosuria while normal non-pregnant persons will usually not do so; (3) the fact that some 90 per cent of gravidæ, following the intramuscular injection of 2 mg. of phlorizin, will show glycosuria, whereas normal non-pregnant persons will seldom do so; and (4) the blood sugar levels of pregnant women both with and without antecedent ingestion of glucose.

The incidence in which glycosuria is met in pregnancy will naturally vary with a number of factors, such as the dietary intake during the three hours previous to voiding, the number of analyses done in the course of pregnancy, the ability of the analyst to detect minor color changes in the test tube and his criteria for a positive test. Actually, the incidence as reported varies tremendously. If, as with lactose, we limit our consideration of glycosuria to cases showing 100 mg. per cent or more (that is, yielding a positive Benedict reaction), the frequency, as reported in the past two decades, ranges between 5 and 35 per cent. In 640 unselected pregnant women Williams and Wills found that 5.4 per cent of the cases were glycosuric. They believe that this figure must represent a close approximation to the true incidence as the series was fairly large and many of the

cases were subjected to repeated examination. Rowe, Gallivan and Mathews, in a series of thoroughly studied and well controlled patients, seen at rather frequent intervals, found that 35 per cent showed sugar at some time during the ante-partum period. Only 18 per cent showed repeated recurrence of glycosuria, and with the majority of these, there were aglycosuric intervals throughout the course of pregnancy. Employing especially delicate methods, Richardson and Bitter have demonstrated that 90 per cent of pregnant women show minute amounts of glucose in the urine (average 38 mg.), whereas on the twelfth day post-partum only 42 per cent exhibit this phenomenon. Even in cases showing a positive Benedict reaction, the amounts of glucose excreted by non-diabetic gravidæ are invariably small, being in most cases just enough to give a faint reaction with the test, that is, of the order of 150 to 200 mg. per cent. Occasional cases may excrete as much as 5 or 6 gr. in twenty-four hours, but larger quantities than this, in the absence of diabetes, are extremely rare.

The ingestion of glucose, levulose or galactose, by pregnant women is so commonly followed by sugar in the urine that several tests for pregnancy have been based on this phenomenon. In 1920 Frank and Nothmann reported thirty cases in the first trimester of pregnancy in which glycosuria was produced by feeding 100 gm. of glucose; in three cases which were later found to be not pregnant, no glycosuria could thus be produced. About the same time Long and Hirst concluded that ingestion glycosuria was a valuable aid in the diagnosis of pregnancy. Gottschalk and Strecker gave 100 gm. of levulose and regarded the presence of levulosuria as diagnostic of pregnancy, though a negative result was not thought to exclude it. Similarly, Rowe has shown that the pregnant woman has a lowered tolerance for galactose since she can tolerate only 20 gm. of this sugar without its excretion in the urine, whereas normal persons can ingest 40 gm. without galactosuria. In 1921 Kamnitzer and Joseph, wishing to utilize glycosuria as a diagnostic test for pregnancy and desirous of avoiding the uncertainties of alimentary absorption following the ingestion of glucose, endeavored to induce artificial glycosuria by the injection of phlorizin. This drug produces glycosuria through interfering with the reabsorption of sugar by the kidney tubules, the exact site of action being apparently the epithelial cells lining the proximal convoluted tubules. If the dosage is reduced to 2.0 or 2.5 mg., the great majority of gravidæ will manifest glycosuria within an hour; whereas non-pregnant persons will seldom do so. Kamnitzer and Joseph reported 300 cases in which this method was used as a test for pregnancy with only six contradictory results. Subsequent studies by various authors showed an accuracy in the neighborhood of 90 per cent. Compared with the later Aschheim-Zondek test and its modifications, the phlorizin procedure is obviously less dependable, but the results obtained with it show clearly the decided tendency of pregnant women toward glycosuria.

Sugar tolerance curves on normal pregnant women indicate that this tendency toward glycosuria is the result of a reduced renal threshold for glucose upon which there may be superimposed a diminished tolerance for sugar. John found that the average renal threshold in pregnancy was but 117 mg. per cent, in contrast

to an average of 149 mg. per cent in normal, non-pregnant persons. Richardson and Bitter carried out sugar tolerance tests on 247 antepartum patients at various stages of pregnancy. Sixty per cent of the women were normal both in respect to their blood sugar curve and in regard to the absence of sugar in the urine. The second largest group, 20 per cent, showed a normal blood sugar curve indicating a normal metabolism of carbohydrate, but the patients in this group excreted sugar into the urine from a blood sugar definitely below the normal kidney threshold. A certain number with sugar in the urine had a maximal blood sugar at some time during the two hours of only 0.140 to 0.150 per cent, and many were not above 0.120 per cent. Williams and Wills believe that the renal threshold must be definitely lowered in the majority of gravidæ, since 60 per cent of their cases showed sugar leaks after the ingestion of 100 gm. of glucose. Elias, Güdemann and Roubitschek have shown in a series of observations on pregnant women that in the earlier months, though the rise in the blood sugar curve after the intravenous injection of glucose is practically the same as in normal non-pregnant women, the leak point is definitely lowered. This was determined by a series of simultaneous sugar estimations in blood and urine, the latter obtained by continuous catheterization. Faber has reported two cases in which, during pregnancy, the sugar threshold was at a level of about 130 mg. per 100 cc. Some months after delivery the threshold in one patient had risen to 150 mg. and in the other to 200 mg. In keeping with this general viewpoint Rowe, Gallivan and Mathews have shown that the blood sugar is at low normal or slightly subnormal levels throughout pregnancy and returns to mid-normal levels early in the postpartum period; their average figure for blood sugar in pregnancy is 83 mg. per cent, for several weeks postpartum 94 mg. per cent.

While there is general agreement that pregnancy is frequently associated with a reduction in the renal threshold for sugar, most students of the subject believe that there is often also a lowered tolerance for sugar. Thus, in Richardson and Bitter's study 8 per cent of the gravidæ showed a blood sugar curve upon which a diagnosis of lowered carbohydrate tolerance would usually be made. In the opinion of Williams and Wills the lowering of the renal threshold, though a factor in all the glycosuric cases, is not the major one in the causation of the glycosurias of pregnancy, but rather it is the association of the lowered renal threshold with an abnormally raised blood sugar curve. Only four of their twenty-one cases of glycosuria were simple renal leaks, the remaining seventeen showing a glucose tolerance curve which, while not diabetic in type, approximated an exaggerated "lag" curve. This tendency of the sugar tolerance curve in pregnancy to lag slightly was brought out as early as 1923 by H. Gray who compared the glucose tolerance curves of 300 normal non-pregnant persons with 50 gravid women. The standard test was performed as follows: a fasting blood was taken followed by the administration of 100 grams of glucose by mouth; blood specimens were then secured after 30 minutes, one hour, two hours and three hours. His average blood sugar percentages for the normal non-pregnant group were: 0.09, 0.14, 0.12, 0.11, and 0.09; and for the pregnant group, 0.09, 0.14, 0.14, 0.12 and 0.13.

Although the consideration given above to the so-called "benign" glycosuria

of pregnancy may seem out of proportion to its clinical significance, the actual importance of the phenomenon both from a practical and theoretical viewpoint is substantial. In the first place, the fact is clear that fasting blood sugar determinations, and often glucose tolerance tests, are essential in all glycosuric pregnant women in order to rule out or establish the diagnosis of diabetes mellitus. In the second place, the "lag" type of glucose tolerance curve so frequently met in gravid women suggests that *there is active, even in normal pregnancy, some process which tends to reduce somewhat the sugar tolerance*. From this it might be anticipated that diabetic gravidæ would often require, other factors being equal, an increased dosage of insulin; that this surmise is correct will be demonstrated in a subsequent part of this review. Of even greater clinical importance, perhaps, is the question: are these women who show glycosuria in gestation, particularly those with a "lag" type of tolerance curve, subclinical diabetics? Edward Allen, as well as Miller, Hurwitz and Kuder, would answer this question most definitely in the affirmative. The former found, upon reviewing the previous obstetrical histories of a group of diabetic women, that they had been delivered of a high percentage of giant babies and of stillbirths long before their clinical diabetes had become manifest. In a more recent investigation of the previous obstetrical histories of a large number of diabetic women, Miller, Hurwitz and Kuder discovered that an increased stillbirth and neonatal mortality (characteristic of diabetes) was demonstrable fifteen to twenty years before the clinical symptoms and signs of diabetes could be recognized. Indeed, during the five years immediately preceding the onset of diabetic symptoms, the stillbirth and neonatal mortality was just as high as after the disease had become established. In keeping with this fact was their further observation that infants with a birth weight of 5000 gm. or more are born to women before they become diabetic with the same high frequency as after diabetic symptoms have appeared. The findings of Miller, Hurwitz and Kuder indicate, moreover, that the presence of glycosuria in the last months of pregnancy, in women whose carbohydrate metabolism is otherwise apparently normal, is also associated with a high fetal and neonatal mortality, similar to that associated with definite signs and symptoms of diabetes. In the light of these observations, pregnancy, with its tendency to lower sugar tolerance, might be regarded as an exceedingly delicate test for subclinical diabetes. There is not general agreement, however, about the validity of these findings. Thus, Dolger and Herzstein, in a review of the records of 200 diabetic married women, found in the twenty-year period prior to the onset of the disease that the stillbirth and neonatal mortality was not significantly greater than for normal patients. However this may be, the practical inference to be drawn from these observations would seem clear, namely, that *the so-called "benign" glycosuria of pregnancy may not always be benign* and that patients showing this condition should have fasting blood sugars done at six month intervals for an indefinite period.

There are two deductions, one practical and one theoretical, to be drawn from the lowered renal threshold for sugar which pregnant women so often exhibit. Unless frequent blood sugar determinations are done, hypoglycemia episodes are

likely to occur. Some gravidæ, it will be recalled, show glycosuria at blood sugar levels under 120 mg. per cent and in such cases reliance on urinary sugar in calculating insulin dosage may be very misleading. In many of these patients it will be found best to forego any attempt to rid the urine entirely of sugar and allow a slight glycosuria. From a theoretical viewpoint it is interesting to note that the cause of the reduced renal threshold is a diminished capacity of the epithelial cells lining the proximal convoluted tubules to reabsorb sugar. The extensive evidence upon which this statement is based has been the subject of three recent reviews, one by Mirsky and Nelson, one by Bock, and one by McKee and Hawkins. The localization of this phenomenon in the renal tubules is noteworthy in relation to the general physiology and pathology of pregnancy since in eclampsia the kidney tubules, particularly their convoluted portions, show degenerative lesions. It would appear that the renal tubules are particularly vulnerable to the changes of pregnancy.

*Diabetes mellitus.* It is an old rule that every patient who shows sugar in the urine should be regarded as a diabetic until proved otherwise. In pregnancy, of course, the frequency of renal glycosuria and lactosuria, throws the odds against diabetes as the most probable diagnosis, particularly if the amount of sugar found is merely a trace. Nevertheless, the above rule should be observed in gravidæ as in other patients because if it is not followed, diabetics are certain to be overlooked through the erroneous assumption that any urinary sugar found is due either to lactosuria or a lowered sugar threshold. This means routine fermentation tests and, if these are positive, routine fasting blood sugar determinations and/or tolerance tests in all pregnant women showing sugar in the urine. By general consensus the diagnosis of diabetes mellitus is established if the fasting blood sugar reaches 0.13 per cent or if, after a meal or during a glucose tolerance test, it reaches 0.17 per cent; if capillary blood is used the latter value is changed to 0.20, the former remaining the same. Since errors in chemical analyses do occur occasionally, all values indicative of diabetes should be confirmed on a second blood specimen.

#### EFFECT OF PREGNANCY ON DIABETES

Pregnancy makes diabetes more difficult to control due to the interaction of a number of factors. These may be outlined as follows:

##### I. Changes in sugar tolerance.

- (a) Sugar tolerance is often diminished (more insulin required) due presumably to increased activity of the anterior pituitary gland.
- (b) Sugar tolerance is sometimes increased (less insulin required) due either to activity of fetal pancreas or to other factors.
- (c) Vomiting, with loss of unknown amounts of carbohydrate food may simulate raised sugar tolerance, may provoke acidosis, and in any event confuses the dietary picture.
- (d) During labor the muscular exertion entailed may so deplete the glycogen reserve that sharp alterations in carbohydrate and insulin requirements ensue.

- (e) A gain in sugar tolerance often occurs after delivery and hypoglycemia in the puerperium is very common; it may be associated with sudden and extreme vacillations in blood sugar, due apparently to reconversion of bodily mechanisms to their non-pregnant states. Lactation, with conversion of certain amounts of blood glucose into lactose may also play a rôle. Puerperal infection, even though mild, may precipitate acidosis and coma with great rapidity.

## II. Increased tendency to ketosis.

- (a) The diminished carbon dioxide combining power of the blood in pregnancy makes gravidæ less resistant to acidosis.
- (b) The elevated basal metabolic rate in pregnancy increases the tendency toward acidosis.

*Changes in sugar tolerance.* The changes in sugar tolerance which diabetic women undergo in pregnancy are neither constant nor predictable; nor are they always in the same direction. In most instances they are in the form of a lowered sugar tolerance in the latter half of pregnancy. In Duncan and Fetter's eighty-four cases gathered from the literature, 56 per cent showed a lower sugar tolerance as pregnancy advanced (i.e., they needed more insulin); 19 per cent exhibited no change; while 25 per cent manifested an increased sugar tolerance (i.e., they required less insulin). Skipper, who made careful observations on seventeen women throughout eighteen pregnancies, found that in thirteen of these the diabetes undoubtedly became worse necessitating an increase in the dosage of insulin. On the other hand, one case showed such marked improvement that it was possible to increase the diet by over 500 calories and to reduce the insulin by one-half. In four patients the tolerance remained unaltered during pregnancy. Brandstrup and Okkels, in a series of eighteen diabetic pregnancies in which insulin was needed, observed that the insulin requirements were increased in four (22 per cent), unchanged in eight (44 per cent) and decreased in six (33 per cent). In Barnes' series of sixteen cases the insulin requirements were increased in fourteen (87 per cent), unchanged in four and decreased in one.

In considering the possible causes of the reduction in sugar tolerance which frequently occurs in pregnancy, it is instructive to recall that there are three other periods in a woman's life when sugar tolerance is diminished and diabetes aggravated. These are the time of puberty, the time of menstruation and the time of the menopause. Priscilla White points out that the onset of diabetes in the female occurs most frequently at ages forty-five to fifty-five and at ages eleven to thirteen; she has found, moreover, that diabetes is more difficult to control during menstruation and at the time of the menopause. The same author studied the cycles of twenty-four diabetic girls at camp one summer. With an almost unchanged diet and insulin dosage, the glycosuria appeared to be greatest in the pre-menstrual and menstrual periods falling to low levels between days seven and twenty-one. Rosenbloom observed a daily glycosuria of 10 to 22 gm. during menstruation in two females who ordinarily were free from glycosuria. Peperkorn has reported two cases of diabetic acidosis occurring during menstruation. Although both of his patients improved, their condition became aggra-

vated again at the following menstrual period. This author states that he has observed fourteen cases in which diabetes became worse at the menstrual period. A comparable, though less marked lowering of carbohydrate tolerance has also been noted in normal, non-diabetic women during menstruation. Thus, Block and Bergel found that the fasting blood sugar in sexually mature females reaches its lowest level in the intermenstruum, gains its maximum on the first day of bleeding, and then returns to the intermenstrual level at the end of menstruation. Similar findings have been reported by Cramer, Pucher and others.

The four periods of a woman's life at which carbohydrate tolerance tends to be lowered, namely, puberty, menstruation, pregnancy and the menopause, are all, of course, times of intense endocrine change and all are associated with increased activity of the anterior lobe of the pituitary body. The hypertrophy which this gland undergoes in pregnancy, its well known cellular alterations and the acromegalic stigmata which gravidæ often show, all attest the hyperactivity of this body in gestation.

That hyperactivity of the anterior pituitary body may lower sugar tolerance was long ago suggested by the fact that glycosuria is exceedingly frequent in acromegaly. In 32 per cent of 650 cases reviewed by Atkinson glycosuria was mentioned. That this glycosuria or diabetes is due to hyperfunction of the anterior pituitary seems probable on the basis of various arguments formulated by Davidoff and Cushing: (1) In these cases there is always an acidophile adenoma of the anterior pituitary. (The reviewer would like to recall here that in gestation the so-called "pregnancy cells" of the anterior pituitary, which become so numerous and prominent, are actually acidophils in a high degree of activity. See Severinghaus.) (2) Diabetes usually does not occur in cases of chromophobe adenomas or other pituitary lesions. (3) Partial extirpation of the acidophilic adenomas causes an improvement in the glycosuria. (4) Some of these cases are insulin resistant. (5) Extirpation or irradiation of the pituitary lowers this resistance.

That hyperactivity of the anterior pituitary actually does lower tolerance and aggravates diabetes is now well known as the result of the classical studies of Houssay and his associates. They have shown: (1) In the absence of the pituitary (or the anterior lobe) pancreatic and phlorizin diabetes is attenuated and animals retain and consume glucose. (2) Anterior pituitary lobe extract counteracts the action of insulin and aggravates pancreatic and phlorizin diabetes. (3) Anterior pituitary extract can produce diabetes in normal mammals. (4) When the pituitary is absent there is a tendency to hypoglycemia, hypersensitivity to insulin and other hypoglycemic agents. These conclusions of Houssay and his collaborators are supported by a series of papers which run into the hundreds; they have been amply confirmed and represent, by general accord, one of the most important contributions which have been made to our knowledge of diabetes mellitus.

It is therefore well established that the anterior lobe of the pituitary secretes a hormone which elevates the blood sugar. It is also believed on the basis of various types of evidence, mentioned above, that this gland is hyperactive in

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have added fourteen cases of their own, making a total series of forty-five cases. Since, prior to 1937, all reported cases of this condition had occurred in diabetic mothers, it was assumed that this islet hypertrophy and hyperplasia was evidence of a compensatory hyperfunction of the fetal pancreas in response to maternal diabetes. However, in 1937 Hartmann and Jaudon reported a case in the absence of maternal diabetes; and in the total series of Potter, Seckel and Stryker, the mother was not diabetic in sixteen or one-third. Moreover, in the majority of cases there was no correlation between the increase of islet tissue and the severity of the diabetes, the state of control or the change in sugar tolerance of the mother during pregnancy. Nor was there appreciable correlation between the amount of islet tissue found at autopsy and the blood sugar levels determined before death in those infants who succumbed during the neonatal period.

All in all, the attempts to prove that the fetal pancreas is responsible for the amelioration which certain cases of diabetes evidence in pregnancy, and to show indeed that it becomes hyperactive toward this end, have been rather unsuccessful. On the other hand, the hypothesis has not been altogether disproved and it remains an intriguing question. More work is needed on this problem. Perhaps an approach by means of experimental alloxan diabetes might prove fruitful.

It is well known that the estrogenic hormone inhibits the gonadotrophic and lactogenic activities of the anterior pituitary gland. In view of this fact it has been suspected that the relatively high incidence with which diabetes mellitus develops at the menopause is the result of hyperactivity of the pituitary gland which is then no longer inhibited by gonadal secretions. This set of circumstances has suggested that the estrogenic hormone may have therapeutic value in diabetes through its depressant action on the anterior pituitary. From the viewpoint of the improvement of certain diabetic women in pregnancy this question is important since the pregnant organism is avowedly flooded with this hormone. Is it possible that a nice balance exists in pregnancy between the diabetogenic factor of the anterior pituitary and the estrogenic hormone with consequent amelioration of diabetes if estrogen blood and tissue concentrations are relatively high, or with consequent aggravation if they are relatively low?

Unfortunately, the several studies which have been published on the effect of the estrogenic hormone on diabetes have yielded contradictory results. Spiegelman has reported that the administration of 10,000 I.U. of estrogenic hormone twice weekly for five months to nine diabetic women was associated with a diminution in insulin requirements, especially in the premenopausal group. Gessler, Halsted and Stetson have reviewed the literature on the effect of estrin on experimental and clinical diabetes and have reported observations on five diabetic women, past the menopause, to whom they had given daily intramuscular injections of 50,000 international units of estradiol benzoate. A significant lowering of the blood sugar resulted in two of the cases in which the onset of the diabetes coincided with the menopause, and probably in a third case in which the menopause preceded the diabetes. In the last two cases there was clearly no effect. In one of them the menopause had preceded the onset of diabetes by at least

pregnancy. These facts are the presumable explanation of the lowered carbohydrate tolerance shown in minor degree by many normal pregnant women, and in major degree by many diabetic gravidæ.

Although changes in sugar tolerance during pregnancy are usually in the direction of a diminution, a substantial minority of all cases reported show an increase in tolerance particularly in the latter part of gestation; and sometimes the reduction in insulin requirements at this time is unequivocal and dramatic. For instance, in a most thoroughly studied case of twins reported by Lawrence, the patient's insulin requirements fell from forty-four units per day at the twenty-seventh week to none whatsoever at the thirty-fourth week. A comparison of her condition before the twenty-eighth week and in the last week showed a gain in carbohydrate tolerance of 100 gr. with more normal blood sugar than before pregnancy. From the low level of the blood sugar there seemed little doubt that more carbohydrate could have been adequately tolerated. This increased tolerance was not maintained after labor.

Obviously, if hyperactivity of the anterior pituitary tends to lower carbohydrate tolerance in pregnancy, in these cases of raised tolerance there must be some opposing factor at work capable of outweighing the diabetogenic glandular effect. It has long been conjectured that this factor is the fetal pancreas. This explanation rests largely on the early work of Carlson and Ginsburg who showed in 1915 that whereas total extirpation of the pancreas in non-pregnant dogs resulted in the onset of diabetes within seven to twelve hours, complete pancreatectomy in four pregnant bitches near term was not followed by hyperglycemia and glycosuria as long as the fetuses were alive and placental connections not severed. At the onset of labor the blood sugar began to rise so that the hyperglycemia, with consequent glycosuria, characteristic of pancreatic as well as severe clinical diabetes, was established on the completion of delivery. Subsequent workers, however, such as Allen, and Markowitz and Soskin, have been unable to confirm these findings.

Attempts to investigate whether insulin passes through the placenta have likewise yielded discordant results. When insulin is injected into the fetus, as was done by Corey and by Pack and Barber, a fall in the mother's blood sugar as well as that of the fetus ensues, but these results may be interpreted in two ways: on the grounds that insulin traverses the placenta and so reduces the maternal blood sugar, or on the basis that it merely reduces the fetal blood sugar level with consequent transudation of maternal blood sugar to the fetus. Actually, of course, in the question at hand, it matters little whether or not insulin passes through the placenta since active fetal utilization of glucose would tend to cause a transudation of sugar from mother to fetus on the presumption that the fetal blood level would then be lower than that of a diabetic mother.

As corroborative evidence that the fetal pancreas plays an important rôle in diabetic pregnancies a number of studies have purported to show the fetal pancreas is hyperactive when the mother suffers from this disease. Potter, Seckel and Stryker have collected from the literature thirty-one cases in which the pancreatic islands of newborn infants showed hypertrophy and hyperplasia and

pregnant diabetic and her infant. As pointed out by Kramer, acidosis is probably more common than generally supposed for it may exist with few or no symptoms. He cites a case of a diabetic gravida in which the carbon dioxide combining power of the blood was discovered on routine study to be but 28 volumes per cent yet the patient had no symptoms whatsoever. Silent acidosis is the cause of many unexplained fetal deaths and, by general accord, acidotic coma is responsible for almost all maternal deaths in this complication. The inherent tendency of pregnant women toward ketosis, therefore, is still another count against them and still another reason why diabetes in pregnancy is more difficult to control.

#### THE EFFECTS OF DIABETES ON PREGNANCY

The effects which diabetes exerts on pregnancy depend in great measure upon the extent to which the disease is controlled. If carefully regulated many of the deadly consequences to the fetus which neglected diabetes regularly imposes, can be eliminated. However, as all statistics show, the disease is potentially inimical to successful pregnancy and even with the best modern care the harmful influences of diabetes often make their appearance, causing a greatly increased stillbirth and neonatal rate. Pregnancy is affected by diabetes as follows:

(a) The incidence of spontaneous abortion and premature delivery is slightly increased.

(b) The frequency of toxemia of pregnancy is greatly augmented.

(c) Fetal death in utero before the onset of labor is much more common than in normal, non-diabetic gravidæ.

(d) The incidence of excessive sized infants is many times that met in normal pregnancies, with the result that mechanical difficulties in labor are more frequent and Cesarean section more often necessary.

(e) Hydramnios is more common.

(f) Congenital malformations are more frequent.

(g) Lactation may be inhibited in some cases.

(h) The neonatal period is associated with especial hazards in the forms of hypoglycemia and anoxia.

*Abortion and premature labor.* Although diabetics may show an increased tendency to abort, the frequency of the accident is well under 20 per cent in controlled cases, that is, definitely less than twice the norm of 10 per cent. Joslin cites the figure of 16 per cent for all cases treated at his clinic since the discovery of insulin and contrasts it with 25 per cent in the pre-insulin era. In Potter and Adair's sixteen cases there were no spontaneous abortions, but there was one case of premature labor at thirty-one weeks and one therapeutic abortion. Among thirty-six cases under the care of Ronsheim, there were only two spontaneous abortions but eight therapeutic interruptions. Skipper's incidence of spontaneous abortion in thirty-seven pregnancies was only 10 per cent. Kramer had three spontaneous abortions in his twenty cases and three therapeutic interruptions.

Since abortion was more frequent in the pre-insulin era, when ketosis was often

seven years; in the other the diabetes had preceded the menopause. Wilder refers to a case of diabetes in which a very significant resistance to insulin developed concurrently with symptoms of the menopause and in which an assay of the urine revealed an excess of anterior pituitary hormone and no estrin. Administering large doses of estrin in this case reduced the requirement for insulin from ninety to fifty units a day. Blood plasma originally obtained from this patient and injected with insulin into rabbits inhibited the action of the insulin. Later, when the patient had been treated with estrin, her plasma was no longer inhibiting. On the other side of the question Lawrence and Maddar failed to demonstrate any effects from doses of 1 mg. of stilbestrol given four times daily for a period of eight weeks to five diabetic women, ages forty-two to fifty-two. Likewise, Salmon and his colleagues, after implanting stilbestrol pellets in eighteen menopausal diabetic women, found an improvement in insulin requirements in only one. Similarly, Collens and his co-workers treated seven cases of diabetes with estrogenic substance and observed little or no effect upon the diabetic state.

In sum, the concensus is against the viewpoint that the estrogenic hormone exerts a favorable effect on diabetes although a few authors believe that it may occasionally do so, particularly at the time of the menopause, when the anterior pituitary is hyperactive. This postulated (but unproven) ability of the estrogenic hormone to suppress the diabetogenic action of the anterior pituitary and so attenuate diabetes should not be confused with the recent hypothesis of the Smiths and Priscilla White which maintains, for quite different reasons, that the estrogens are beneficial also in diabetes complicated by pregnancy. The Smith-White hypothesis will be discussed in a subsequent section of this review.

*Increased tendency to ketosis.* Although ketonemia and ketonuria are rarely found in normal pregnancy, there is a greater liability to ketosis during gestation. C. H. Gray has studied ketonuria in twenty-seven normal pregnant women following a fourteen hour fast and found it present in seventeen, as indicated by the Rothera test; the same number of normal non-pregnant women, fasted in a similar manner, gave negative tests. Similarly, a high fat intake or a carbohydrate-poor diet has a much greater tendency to produce ketonemia and ketonuria in pregnancy than in the non-pregnant state, as shown by the work of Bokelman and Bok and of Kleesattel. Four factors, all of them well established changes of pregnancy, contribute to this tendency. In the first place, the marked reduction in the carbon dioxide combining capacity of the blood in pregnancy reduces its ability to buffer ketone bodies. Secondly, the increased basal metabolism requires additional carbohydrate fuel if the burning of fats is to be forestalled. Thirdly, as shown by Harding and Allin, there is a substantial loss of anti-ketogenic material, in the form of glucose, to the fetus. And, finally, the sharp increase in blood fats, which is a regular accompaniment of pregnancy, is a potential cause of ketosis unless the carbohydrate intake is ample. Tyler and Underhill, as well as Boyd, have compared the lipemia of pregnancy with that seen in diabetes; it is well known that in diabetes hyperlipemia is usually associated with a bad prognosis.

Ketosis and coma constitute the gravest complication which can befall the

to hyperglycemia. Certainly, the excessive size of these infants is not due to prolongation of the pregnancy because, as shown by Fischer, at any given gestational age in the last trimester of pregnancy, the baby of a diabetic is larger, on the average, than the infant of a non-diabetic of the same gestational age.

*Hydramnios.* A common accompaniment of diabetes in the pre-insulin era, hydramnios is infrequent in most modern series of cases being seen, perhaps, in about one case in ten. Most authors regard it as evidence of neglect in that it shows that the fetus has suffered from persistent hyperglycemia. The fetus apparently excretes the sugar above a certain renal threshold into the urine, raising the osmotic pressure of the amniotic fluid and as a result an inflow of fluid from the surrounding tissues occurs. Another explanation is that the hydramnios results from fetal diuresis consequent upon fetal hyperglycemia.

*Malformations.* Congenital malformations of major degree occur in 2 to 3 per cent of the cases reported and constitute a small but definite proportion of the causes of fetal death.

*Lactation.* Although successful lactation has been reported by some authors, such as Peckham, and Wilder and Parsons, others find diabetic patients deficient in milk production. White is emphatic that lactation in diabetics is poor, perhaps because of relative undernutrition or lack of the specific lactogenic hormone. In the reviewer's clinic, most diabetics are able to nurse their babies satisfactorily.

*Neonatal complications.* The blood sugar levels of normal infants are low during the first two days of life, ranging according to Ketteringham and Austin between 55 and 75 mg. per cent. McKittrick regards any value above 40 mg. per 100 cc. as normal during the first week. In the babies of diabetic mothers the blood sugar concentrations fall to even lower levels in about a quarter of the cases. Since the fetal pancreas in diabetic mothers is believed to be hyperactive, this marked fall in the blood sugar of these newborn is usually attributed to the sudden removal of maternal sugar in the presence of a very active pancreas. Although a few deaths have been reported in newborn infants of diabetic mothers and attributed to hypoglycemia, the most careful students of the subject doubt if low blood sugar is ever the actual cause of exitus in such babies unless insulin is given the mother shortly before birth. White, Sisson, as well as Hanley, Horn and Farmer, agree on this point.

All observers have noted that the behavior of many babies of diabetic mothers is abnormal in the early neonatal period, being characterized particularly by lethargy and a tendency to cyanosis. Sisson finds that 43 per cent of such infants manifest abnormal symptoms and that the neonatal death rate is 18 per cent. In his opinion, cerebral anoxia with involvement of the respiratory center is the cause. Miller and Wilson have demonstrated cardiac enlargement roentgenographically in ten infants born to diabetic mothers; this change disappears during the first six weeks. In three of eighteen infants studied at autopsy, macrosomia, cardiac hypertrophy, hemopoiesis in the liver and hyperplasia of the islands of Langerhans were demonstrated,—alterations similar to those found in erythroblastosis fetalis.

difficult to eliminate, it is a reasonable supposition that acidosis predisposes to abortion and may be a factor in the slightly increased incident of the accident today. The presence of a lethal gene and also dietary deficiencies have also been advanced as explanations.

*Toxemia of pregnancy.* All authors agree that the frequency of toxemia of pregnancy is greatly augmented. If 7 per cent be taken as the usual incidence of this complication, most reports show a several fold increase: Potter and Adair, 50 per cent; Barnes, 45 per cent; Mengert and Laughlin, 24 per cent; Bill and Posey, 27 per cent; Gaspar, 33 per cent; White, 16 per cent; Lavietes, Leary, Winkler and Peters, 39 per cent.

In the series reported by the last group of authors, toxemia occurred in ten patients. Of these there were four with a history of hypertension before the onset of pregnancy. Five of six patients with pre-eclampsia were twenty-eight years of age or over. Three of the six, including the youngest, had labile hypertension prior to pregnancy. The authors believe that the risk of toxemia is slight in young patients and in multigravidae without previous hypertension or toxemia. In this series there was no correlation between fetal mortality and maternal toxemia. In a study of forty-three pregnancies in thirty-eight diabetics, Edward Allen found that 70 per cent showed one or more signs of toxemia. With the exception of two patients all of his toxemic women weighed between 160 and 240 pounds. The tendency of diabetics to obesity plus the age factor account in large measure for the higher incidence of chronic hypertensive vascular disease in pregnancies complicated by diabetes. In the present state of our knowledge there is no tenable explanation for the increased incidence of pre-eclampsia in diabetics, except as advanced in the Smith-White hypothesis (page 24).

*Fetal death in utero.* It is well known that fetal death in utero prior to the onset of labor is common in diabetics. Kramer found that sixty of 238 cases collected from the literature, or about one-quarter resulted in stillborn infants. Of the nineteen stillbirths reported by Gaspar, twelve were macerated, a fact which would indicate that about two-thirds of their deaths occurred in utero and not as a result of delivery. Toxemia of pregnancy greatly increases the likelihood of fetal death, but many cases are unexplained. The most likely presumption is acidosis. Most of these fetal deaths occur in the last month of pregnancy and it is this fact, of course, which has led to a wide-spread policy of delivering these patients, if at all feasible, two or three weeks before the expected date of confinement.

*Excessive sized infants.* The incidence of babies born to diabetic mothers, weighing ten pounds or more, ranges in the various series reported between 15 and 25 per cent. In the childbearing population at large the frequency of such large babies is approximately 3 per cent. The explanation usually given for the high frequency of large babies born to diabetic mothers is hyperglycemia. However, most authors agree that these infants are not just fat but generally large and it is suspected that endocrine imbalance, particularly in relation to the growth hormone of the anterior pituitary of the fetus, may be a factor in addition

develops and by other factors. Nevertheless, in a noteworthy statistical analysis of several large series of cases, White and Pincus seem to have shown that the appearance of diabetes in family trees approaches closely to Mendelian recessive ratios.

The practical conclusions to be drawn from these findings as summarized by White and Pincus are: (1) If both parents have diabetes the child will almost certainly have it. (2) If one parent has the disease and the other has not, but if in the family of the non-diabetic parent his father or mother has it, there is an even chance that the child will be affected, for the non-diabetic parent is a carrier. If the brother or sister of the non-diabetic parent has diabetes, he may or may not be a carrier, so that the chances of the child developing it are less than even. (3) If neither parent has diabetes but if, on both sides, the disease has occurred in one of their parents, both are carriers and the chances are one in four. If a brother or sister of the parents (on both sides) has diabetes, the parents are probably carriers and the chances are again one in four. (4) If a

TABLE 1

*A comparison of the incidence of diabetes in the siblings of non-diabetics, diabetics, dissimilar and similar twins, and of diabetes in their parents (From White and Pincus)*

TYPE OF POPULATION	SIBLINGS NUMBER	PER CENT DIABETIC	PER CENT PARENTS DIABETIC
Control.....	862	0.6	2
Diabetic.....	2,835	5.0	9
Dissimilar twin.....	29	7.0	10
Similar twin.....	19	63.0	5

child of parents, who do not themselves have diabetes, develops the disease, the parents are probably carriers and the chances are probably one in four that any other children will develop it. (5) The chances of a diabetic and a true non-diabetic reproducing a diabetic are nil, but 25 per cent of the population are said to be carriers.

When diabetes occurs in three generations of a single family it may appear earlier in the second than in the first and earlier in the third than in the second. When an inheritable character makes its appearance in one generation of a single family at a given age and in the following generation at any earlier age and so on, the phenomenon is known as anticipation. In a study of 100 families which showed diabetes in two generations, Woodyatt and Spetz encountered unquestionable anticipation in sixty-four cases, the differences between the ages of onset in the two generations ranging between ten and fifty years. In ten of eighty-eight families that showed the disease in two generations the diabetes skipped one generation, occurring in the first and third generations. In these families the differences in the ages of onset in the first and third generations varied from twenty-five to sixty-five years. In all the families that showed the trend (only seven of the 100 families showed the reverse), the average difference between the age of onset in the two generations was twenty years. In all those

In addition to the direct effects of diabetes upon pregnancy, as described above, there are two other factors present in most diabetics which influence pregnancy deleteriously in an indirect way. These are age and obesity. At the risk of repetition let it be recalled that the average age of diabetic gravidae in all series reported is in excess of thirty years and that the majority are overweight. The important rôle played by obesity in the etiology of excessive sized infants, malpresentations and toxemia is of course well known.

#### PROGNOSIS

Although Skipper in 1933 found a maternal death rate of 9.3 per cent in 136 post-insulin cases collected from the literature, this is much higher than is reported in most recent series. Thus, the following series record no maternal deaths: Kramer, 20 cases; Laviates, Leary, Winkler and Peters, 31 cases; Mengert and Laughlin, 33 cases; Brandstrup and Okkels, 22 cases; Gaspar, 49 cases; Barnes, 25 cases. In 1935 Kramer collected 238 cases from the literature with eight maternal deaths, that is, a maternal mortality rate of 3.0 per cent. *Almost all maternal deaths today from diabetes complicated by pregnancy are due to neglect.* For instance, in the series of Potter and Adair, comprising 16 pregnancies, their one maternal death occurred in a woman admitted to the hospital in coma, who had had no prenatal care and who died undelivered a few hours after admission to the hospital.

The prognosis for the child in diabetes complicated by pregnancy is implicit in the two foregoing sections and will not be repeated here.

#### THE HEREDITY OF DIABETES MELLITUS

The hereditary nature of diabetes mellitus was recognized as early as the turn of the century and has itself been the subject of a large literature. In the present review only those aspects of the topic will be considered which are of clinical importance, that is, those having to do with the likelihood that the offspring of a given mating will have diabetes. For a more complete survey the reader is referred to the article of White and Pincus.

The hereditary etiology of diabetes rests upon several types of evidence: (1) Diabetes in twins. As show in table 1, from White and Pincus, the frequency of the disease in both members of pairs of identical twins far exceeds the incidence in fraternal twins, as would be expected in a hereditary disease; and, in turn, the frequency of diabetes in fraternal twins and siblings of diabetics is many times that encountered in the population at large. Other studies on diabetes in twins show similar findings. (2) The excessive incidence of diabetes in blood relatives of diabetics. In an analysis of 4,434 parents and siblings of diabetics and 1,290 parents and siblings of non-diabetics, the same authors found that the total incidence of diabetics in the former group was 6.7 per cent as compared with 1.23 per cent in the latter. (3) Demonstration of Mendelian ratios of the recessive type not only in actual diabetic families but in presumably latent diabetics. Evidence of this type is difficult to establish because expected ratios are altered by the fact that some potential diabetics die before the disease

During the first trimester, nausea and vomiting may prevent the patient from adhering to her usual diet and insulin dosage. If vomiting is severe, acidosis may become extreme and control precarious. As Potter and Adair point out, this is a circumstance in which therapeutic abortion may sometimes become mandatory. Immediate hospitalization is obviously required in such cases followed by estimations of the blood sugar and carbon dioxide combining power of the blood. Many of these patients are best treated by hourly feeding and administration of ordinary insulin at three-hour intervals. If the vomiting is marked, glucose must obviously be given intravenously with the necessary ordinary insulin to cover and the procedure repeated as indicated.

During the last trimester vigilant observation must be maintained for evidence of shifting sugar tolerance and for signs of beginning pre-eclampsia. Changes in insulin dosage must be made cautiously since any sharp increases may subject the patient to hypoglycemic reactions. All authorities agree that if an error is to be made in insulin dosage it should be in the direction of a slight glycosuria. During labor, because of the glycogen demands on the liver, it is well to give the equivalent of 10 gr. of glucose every hour or so.

Upon the patient's final admission to the hospital three weeks or so before term, two important obstetrical decisions must be made: when to effect delivery and how. Because of the tendency of the fetus to succumb as term approaches, and for other reasons, there is a widespread but far from unanimous belief that pregnancy should be terminated by Cesarean section before the last fortnight of gestation. Thus, on the one hand, Titus, Ronsheim, Randall and Ryncarson, and other authors recommend routine Cesarean section two or three weeks before term; on the other, Hurwitz and Irving, Mengert and Laughlin, Laviates, Leary, Winkler and Peters, as well as others, perform Cesarean section only when indicated and not because of diabetes. In between stand another group who employ abdominal delivery much more frequently in this complication; for instance, Bill and Posey's incidence of the operation was 32 per cent. Advocates of Cesarean section point out that the infant is likely to be large (60 per cent over 8 lbs.) with consequent mechanical difficulties in labor, that such babies with their inherent tendency to anoxia stand labor poorly and that this operation, performed a fortnight before term, forestalls the ever-present likelihood of fetal death in utero. Against this viewpoint is the contention that diabetics are poor operative risks and that the outlook is equally good with vaginal delivery provided the disease is well controlled.

As implied above, it is the reviewer's practice to admit all diabetic gravidæ to the hospital three weeks or so before term not only for stabilization of the diabetes but for consideration of the whole problem of delivery. After it is established that the diabetes is well regulated, the size of the infant is estimated as accurately as possible by palpation and a sterile vaginal examination done. The purpose of the latter is to answer the question: Is the cervix favorable for the induction of labor? An affirmative answer is given to this query if (1) the head is at or below the spines, (2) the cervix admits easily one or more fingers and (3) the cervical canal is less than 1 cm. long. If all three of these criteria are present and provided the infant is thought to weigh between 3000 and 3500

that showed anticipation between the first and third, or second and fourth generation (the intervening generation having escaped diabetes), the average difference was forty-five years, or twenty-two and a half years per generation of family.

These findings of Woodyatt and Spetz are not without their clinical bearing. If the age of onset of diabetes in a parent should be thirty years, the child of the parent (or nephew or niece) developing the disease would do so in a large majority of cases at an earlier age and, on the basis of the averages found in their series, at about the age of ten. Accordingly, if the child should be unaffected at the age of ten, the probability that he would develop the disease would diminish with every passing year, until at the age of thirty it would become rather remote.

The tendency of diabetes to develop at a genetically determined time is well shown by White's forty-eight cases of twins in fourteen of which the disease appeared in both members of the pair. In eleven of these, or about 80 per cent, the ages of onset were 2-3, 5-8, 3-13, 9-12, 17-29, 47-52, 53-55, 56-63, 57-57, 60-62 and 62-62 (greatest spread twelve years). The three other cases (20 per cent) showed greater variations, e.g. 35-60, 29-67 and 19-67.

#### MANAGEMENT

*Management of the mother prior to delivery.* The main objective in the management of diabetes complicated by pregnancy is *rigid control of the disease*. This is the responsibility of the internist, who should share jointly with the obstetrician the care of every such case. Once the diagnosis of diabetes is established the patient should be admitted to the hospital for careful evaluation of the diabetic status. She should be admitted again for the same purpose every other month throughout pregnancy and oftener if she shows evidence of a fluctuating carbohydrate tolerance. It is usually unnecessary for these hospital stays to exceed three days, but occasionally control of the disease proves so difficult that hospitalization is required for a fortnight or longer. In addition, ambulatory visits to the internist and the obstetrician are made at two-week intervals and blood sugar determinations carried out, either fasting or post-prandial. Three weeks before term, in the opinion of the reviewer, the patient should again be admitted to the hospital to remain there until after the baby is born. The purpose of this admission is two-fold: stabilization of the diabetic preparatory to delivery and consideration of the desirability and possibility of early delivery.

As has been emphasized repeatedly in this review, blood sugar levels and not urinary sugar must determine the diet and insulin dosage recommended. Internists such as White and Sindoni, agree that a rather liberal carbohydrate intake is desirable as a preventive against ketosis. White's recommendations are: 30 to 40 calories per kilogram, carbohydrate 150 to 250 grams, protein 2 grams per kilogram and fat to complete the caloric prescription. Sindoni finds that an average safe diet for the total day is 60 grams of protein, 80 to 90 grams of fat and 150 to 180 grams of carbohydrate; he advocates, however, an extra feeding upon retiring of 15 to 20 grams of carbohydrate. The same author employs protamine zinc insulin in those patients requiring more than 40 units of plain insulin, but seldom alone, because of the dangers of hypoglycemic reactions during the interval between meals.

whose mothers' gonadotrophin values rose steadily to term. In 1940 White reported the treatment of eleven diabetic gravidæ with oral stilbestrol in dosages of 40 to 120 mg. daily and pregnolinine, 10 to 40 mg. daily with a fetal survival rate of 90 per cent.

In the opinion of White gigantism of the baby may also be related to the abnormal hormonal balance in that the weights appeared to have been controlled in the treated group. As a basis for this contention she cites the work of Snyder who injected chorionic gonadotrophin into pregnant rabbits and "produced a result not unlike a diabetic pregnancy, miscarriage, stillbirth, overdevelopment, death and maceration of the giant fetus!"

The claims of White in regard to the important rôle played by elevated chorionic gonadotrophin in diabetes complicated by pregnancy may be evaluated on two grounds: (1) the underlying rationale and (2) the actual lowering of fetal mortality achieved by treatment. The underlying rationale would seem open to question for a number of reasons: (1) The endocrine etiology of pre-eclampsia as postulated by the Smiths awaits confirmation. Taylor and Scadron have also studied the serum gonadotrophin in late pregnancy but conclude that the general average and range of the gonadotrophin concentration in toxemic patients were not significantly different from normal controls. (2) In regard to Snyder's production of macerated, giant fetuses by the injection of chorionic gonadotrophin, this was accomplished as the title of his paper indicates, through *prolongation* of rabbit pregnancies with continued growth of the fetuses for at least three days beyond term. Naturally, the fetuses were excessive in size with this period of overgrowth, which corresponds in the human to a post-maturity of about one month. The giant fetuses of human diabetics are not the result of prolongation of pregnancy; indeed, they are often encountered a week or more before term. Then, there is another respect in which this analogy with Snyder's work is inept. The mechanism underlying the action of chorionic gonadotrophin in Snyder's rabbits was ovulation with resultant formation of fresh corpora lutea. It was, of course, the progesterone manufactured by these fresh corpora lutea which caused prolongation of the pregnancy and the giant fetuses. In other words, if chorionic gonadotrophin produces giant fetuses in rabbits it does so through the production of additional progesterone. This is the very substance recommended by White to prevent giant fetuses. It would hence seem to the reviewer that Snyder's observations have no bearing one way or another on White's contentions. (3) If elevated chorionic gonadotrophin and low estrogen cause premature labor, it seems strange that this imbalance does not cause trouble more frequently about the seventieth day of pregnancy when chorionic gonadotrophin is at its highest peak and estrogen is low.

More important than the above considerations, however, is the question: what results have been achieved by the endocrine therapy recommended in a series large enough to be free from sampling error? No such series has yet been reported but an approach to an answer may be had from White's most recent article (1943) in which 125 diabetic pregnancies, treated and untreated, are reported with seventeen fetal and neonatal deaths, a gross infant loss of 13.6

grams, the membranes are stripped back and ruptured. In our last 600 inductions by artificial rupture of the membranes we have had no failures provided the cervix was favorable as indicated by the criteria mentioned. If the cervix is not wholly favorable for induction, the next question asked is: How urgent is immediate delivery? Three findings may indicate that it is very desirable: (1) the presence of an associated toxemia; (2) the presence of an obviously large child; and (3) inability to control the diabetes. In the presence of any of these conditions, Cesarean section is done. If they are not present and the cervix is unfavorable, the patient is allowed to go to term in the hospital or until such time as the cervix is favorable. Naturally, such other factors as elderly primiparity and previous infant loss would also argue for abdominal delivery; contrariwise, marked obesity might serve as a deterrent. Continuous spinal anesthesia is probably the anesthetic of choice if abdominal delivery is performed.

*The Smith-White endocrine hypothesis.* In a series of painstaking endocrine studies George Van S. Smith and O. Watkins Smith have presented evidence which seems to show that the toxemias of later pregnancy are associated with a quantitative imbalance between chorionic gonadotrophin on the one hand, and estrogen and progesterone on the other. They not only find that chorionic gonadotrophin is usually very high in the toxemias and estrogen and progesterone very low but that this shift in balance antedates the actual development of clinical toxemia by some weeks. This demonstration of a typical hormonal imbalance involving an estrogen and progesterone deficiency, prompted the Smiths to administer these two hormones in the hope of re-establishing a normal balance. This therapy has now been employed by them in a substantial number of cases with restoration of proper endocrine balance and, in many instances, this has been associated with amelioration of the clinical toxemia and recrudescence on the cessation of treatment.

Because of the high incidence of pre-eclamptic toxemia and premature delivery in diabetic women, the Smiths concentrated on these patients in following hormonal changes prior to clinical manifestations and in this work had the collaboration of Priscilla White of the Joslin Clinic. The latter worker, convinced of the special applicability of these studies to certain problems encountered in diabetes complicated by pregnancy, has independently carried the work further in this particular field.

In the opinion of White, the abnormal endocrine picture described above, is responsible for the high incidence of toxemia in diabetes, the increased incidence of premature labor and certain other accidents which often befall the child in this disease. Thus, she found that the clinical course of twenty patients whose values for serum gonadotrophin were normal, was completely uneventful. None developed toxemia. None miscarried. Quite different were the clinical courses of eleven patients whose values for serum gonadotrophin were elevated and who received no therapy. All developed complications. Eight developed toxemia. The remaining three delivered themselves prematurely. In contrast to the low mortality rate of 5 per cent in infants of diabetic mothers whose values for serum gonadotrophin were normal was the high rate of 55 per cent (6 cases) in the eleven

whose mothers' gonadotrophin values rose steadily to term. In 1940 White reported the treatment of eleven diabetic gravidæ with oral stilbestrol in dosages of 40 to 120 mg. daily and pregnolinine, 10 to 40 mg. daily with a fetal survival rate of 90 per cent.

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per cent. This is an exceedingly low figure, but it is not substantially less than has been achieved (in smaller series, it is true) by Hurwitz and Irving, 15 per cent, and by Mengert and Laughlin, 18 per cent, without endocrine therapy. Actually, White does not report this gross figure, but divides her patients into those with abnormal endocrine levels (twenty-seven cases) with fifteen infants lost (55.6 per cent); and those who either had normal balance or who received therapy (ninety-eight cases) with only two infant deaths, (2.0 per cent). The former figure is worse than obtained in pre-insulin days and the latter better than most clinics can achieve for total infant loss in non-diabetic women. This suggests sampling errors. For this reason most obstetricians will find these broken-down statistics difficult to interpret and will probably prefer to evaluate the gross figure.

White's work is in need of clinical confirmation or refutation at other hands. B. L. Bowen has reported a single case in which oral administration of 6 mg. of diethylstilbestrol daily resulted in a dramatic reduction in insulin requirements and the disappearance of the signs and symptoms of a mild toxemia. On the other hand, Hurwitz takes issue with White on a number of scores. He points out, on the basis of statements in the articles of the Smiths and White herself, that pregnancy accidents may occur in patients with a normal hormonal balance and that abnormal hormonal balances may revert to normal without treatment. He notes further that in a group of fifty-three pregnant women with diabetes at the Boston Lying-In Hospital, there were only eight fetal deaths, a fetal mortality of 15 per cent. These women received no specific therapy other than for the diabetes and all were delivered in conservative fashion. This mortality rate, Hurwitz points out, compares favorably with the 33 per cent given by White as the usual fetal mortality and with the 13 per cent in her own endocrine-treated series.

*Management of mother in puerperium.* Diabetes may be more difficult to control in the early puerperium than at any other time. The wide and sudden fluctuations which the blood sugar sometimes undergoes during this period are presumably the result of a number of factors: endocrine and metabolic changes associated with the reconversion of bodily mechanisms to their non-pregnant state, slight degrees of puerperal infection, conversion of certain amounts of blood glucose into mammary lactose and possibly the sudden withdrawal of the fetal pancreas. Disturbances in sugar tolerance are most common during the first week postpartum after which the diabetes returns rapidly to its pre-pregnancy status. There is no evidence that pregnancy ever causes permanent aggravation of diabetes.

As a basis for insulin dosage daily blood sugar determinations should be carried out during the first week postpartum. Here, as in vomiting of pregnancy, because of the unpredictable vacillations in blood sugar, three or four injections of ordinary insulin a day, with food to cover, are often preferable to the longer acting protamine zinc insulin. And, in general, when diabetes in pregnancy, labor or the puerperium, becomes troublesome to control, the difficulties are more easily met, as a rule, with frequent doses of ordinary insulin than with the protamine zinc variety. As has already been stressed, care must be exercised to differen-

tiate between urinary glucose and lactose since both may be present in substantial quantity and both reduce Benedict's and Fehling's solution.

Although there is a divergence of opinion on the desirability of lactation, the majority of authors favor it and seem to meet little difficulty in establishing satisfactory nursing. In this connection Sindoni stresses the care which must be exercised in the management of the mother's diabetes when weaning the child. Blood sugars must be checked frequently at this time to prevent hyperglycemia or acidosis. Sindoni cites two patients in his own experience who were admitted to the hospital in diabetic coma while they were in the process of weaning their infants. One had been lactating five months, the other fifteen months.

*Management of the infant.* Two special problems present themselves in the management of the newborn infant of a diabetic mother: hypoglycemia and anoxia. In order to forestall the former Randall and Rynearson, in a notable article on the subject, recommend the injection of 5 cc. of 10 per cent glucose into each buttock a few minutes after birth. Further such injections are given at intervals regulated by the value of the blood sugar as determined by the micro-method, by the behavior of the infant and by the ability of the infant to take feedings by mouth. The same authors attempt feeding within four hours, giving either 10 cc. of a 10 per cent solution of glucose or 7 cc. of a karosyrup lactic acid mixture every two hours during the first two or three days. Whenever the feeding is taken poorly or whenever twitchings, convulsive movements or cyanosis indicate, in the opinion of the authors, the development of hypoglycemia, 10 cc. of a 10 per cent solution of glucose is given by mouth if possible; otherwise it is administered intramuscularly.

Although Randall and Rynearson report seven cases in which hypoglycemia appeared to cause convulsions and cyanosis, and even threatened the life of the infant, there is a substantial body of opinion to indicate that these authors over-emphasize this danger. As already stated, the blood sugars of many normal newborn infants fall below 50 mg. per 100 cc. without untoward signs of any nature; and in the opinion of White, Sisson, Sindoni and others, the twitchings, cyanosis and convulsions which infants of diabetic mothers sometimes manifest, are related to the inherent tendency of these babies to anoxia rather than to hypoglycemia. However this may be, it is the custom of most authors to give these infants glucose, either by mouth or intramuscularly at frequent intervals during the first three days, although it may well be unnecessary. It can do no harm and may prove helpful in occasional cases. Obviously, because of the tendency of the newborn to hypoglycemia, insulin should not be given to the mother during the three hours immediately preceding delivery.

During the first few days of life the infants of diabetic mothers should be given the same treatment which premature babies receive in respect to oxygen and heat. This means placing them in an incubator with oxygen flow regulated to provide a partial pressure of oxygen between 40 and 50 per cent. The temperature should be about 85°F. and sufficient nursing personnel available to permit constant observation during the first seventy-two hours. Their care, of course, should be the responsibility of a pediatrician.

*The problem of future pregnancies.* From the viewpoint of cold logic, diabetic

women should not become pregnant. The increased risk to the mother, the greatly increased hazards faced by the infant and the very patent eugenic implications, all support this statement: However, as every obstetrician knows, factors other than reason, are frequently interjected and some compromise with the above injunction must often be made. In so far as the maternal and fetal risks are concerned, these would not appear so great as to preclude the bearing of two or three children. In some 75 per cent of cases, by the law of probability, the husband will be a true non-diabetic, that is, neither he, his siblings, nor any member of his family in the two preceding generations, will show a history of diabetes. In such matings there is practically no chance of the child developing the disease but he or she will be a carrier. If the husband is a carrier and particularly if he himself is a diabetic, childbearing would seem most reprehensible. On the other hand, we have the authority of Joslin on this question as follows: "With improvement in the management of the disease less and less danger of invalidism and premature death will be involved. Moreover, who will be left to halt the falling birth rate if all unsound individuals in the country are forbidden to have children? There are many individuals one meets on the street who are far less desirable to choose for fathers and mothers than diabetics." All in all, so many factors—medical, eugenic, social, religious and sentimental—bear on this problem, that the decision would seem best left to the circumstances of the individual case and the conscience of the physician.

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# PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

## RELATION BETWEEN GASTRIC ACIDITY AND THE ANTERIOR-PITUITARY-LIKE HORMONE CONTENT OF URINE IN PREGNANT WOMEN

STANLEY WAY

Brit. Med. Jour., 182-184, August 11, 1945

The author recalls that numerous observations on gastric acidity in pregnancy show that there is a striking diminution in both free and total acid content of gastric juice in response to a test meal. Previous investigations, moreover, have drawn attention to the fact that the lowest secretion of free acid coincides with the period of pregnancy when nausea and vomiting are common. In 1938, during a statistical investigation into the incidence of hyperemesis gravidarum, the author noticed an extraordinarily high incidence of this disorder in patients who were suffering from hydatidiform mole. Since hydatidiform mole is associated with the presence in the urine of large amounts of anterior-pituitary-like hormone, it appeared to the author that this hormone might be responsible for the low secretion of acid in the gastric juice. Since it is well known that the secretion of anterior-pituitary-like hormone reaches its maximum between the 56th and 84th days, and since the investigations mentioned above indicate that the diminution in gastric acidity is most pronounced at about this time, the author's suspicion that there was a relationship between these two phenomena seemed plausible.

Moreover, soon after this work was started, an important piece of experimental evidence was published by Culmer, Atkinson and Ivy (1939). They showed that in dogs with Pavlov pouches, the secretion of free and total acid could be very greatly diminished, even after histamine, by the injection of fairly large amounts (1,000 to 5,000 rat units) of anterior-pituitary-like hormone. They were unable to produce this effect with any other hormone known to be secreted in excess during pregnancy.

In the present investigation the relationship between free and total acid in response to a test meal and the secretion of anterior-pituitary-like hormone in the urine was studied. The subjects were 67 women who gave no history of gastric disorders. Twenty-two were between the 35th and 40th weeks of pregnancy; 20 between the 20th and 29th weeks; 21 between the 8th and 16th weeks; 1 had a missed abortion; 1 had a dead fetus at full term; 1 had a hydatidiform mole; and 1 a chorionepithelioma. Samples from twenty-four hour specimens were taken and Aschheim-Zondek reactions were performed on undiluted samples of urine, on samples diluted 1 in 5 and 1 in 10.

The author was able to confirm in the first place that there is a marked diminution in gastric acidity during the early weeks of pregnancy. Thus, his patients who were 8 to 16 weeks pregnant showed an average maximum secretion of free

HCl of 0.023%; those who were 20 to 29 weeks showed an average maximum secretion of 0.045%, while those who were 35 to 40 weeks pregnant manifested a maximum average secretion of 0.079%. He found in the second place that there was a very definite and inverse relationship between the concentration of anterior-pituitary-like hormone in the urine and the secretion of hydrochloric acid by the stomach. Thus, in the group in which Aschheim-Zondek tests were positive at dilutions of 1 in 10, the maximum secretion of hydrochloric acid was only 0.029%. In the group in which the Aschheim-Zondek test was positive in dilutions of 1 in 5 but negative in dilutions of 1 in 10, the maximum concentration of hydrochloric acid was 0.044%, while in those cases which showed the lowest concentration of anterior-pituitary-like hormone, those in which the Aschheim-Zondek test was positive but negative in any dilution, the maximum secretion rose to 0.079%. The author concludes, accordingly, that there seems to be some relation between the free and total acid in the gastric juice and the amount of anterior-pituitary-like hormone secreted in the urine, and that it seems to be inversely proportional.

(From a clinical viewpoint it is instructive to note that the observations of Way and other authors on the hypochlorhydria of pregnancy carry important implications in regard to the causation of some of the commonest complications of gestation: (1) Diminution in acid contents of the stomach is usually paralleled by a decrease in gastric motility which, in turn, is believed to be the cause of heartburn and flatulence, and may be an etiological factor in hyperemesis; (2) Hypochlorhydria interferes with the ability of the stomach to absorb iron and so predisposes to anemia.

We used to think that heartburn was due to gastric hyperacidity and that it therefore called for sodium bicarbonate as a remedy, but gastric analyses on patients with heartburn regularly show that the great majority of these cases are associated with a relative anacidity. Actually, as demonstrated by Chester Jones (*Digestive Tract Pain*, New York, The Macmillan Co., 1938), N. H. Williams (*Am. J. Obst. & Gynec.*, 42, 814, 1941) and others, the composition of the gastric juice has nothing to do with heartburn, which is essentially a neuromuscular disturbance consequent upon diminished gastric motility. The latter is a constant, "physiologic" accompaniment of pregnancy and results in reverse peristaltic waves and the regurgitation of stomach contents into the esophagus. The irritation of the esophageal mucosa, so produced, causes heartburn regardless of the acidity of the juice. Hence, the main objective in the treatment of heartburn is to improve gastric motility.

In view of the above facts, the beneficial effects which can often be achieved in heartburn by the administration of dilute hydrochloric acid before meals, must be interpreted on the grounds that gastric motility, in general, increases directly with the acid contents of the stomach. The same reasoning applies to the use of dilute hydrochloric acid in flatulence. Employing a similar rationale, N. H. Williams has found that a single injection of prostigmine, 1 cc. of a 1:2000 solution intramuscularly, will usually give relief from heartburn for a week or so. In regard to sodium bicarbonate it is common experience that this remedy is often ineffectual and, at best, gives only temporary relief. It has the additional disadvantage that it increases the quantity of sodium in the body and, if used persistently, may predispose to edema.

The frequency of hypochlorhydria in gestation and its tendency to cause anemia, may well be borne in mind when treating cases of microcytic anemia of pregnancy which respond slowly to the usual iron medication after meals. Supplementing the iron therapy with dilute hydrochloric acid before meals will sometimes help in these cases.—Ed.)

## THE TRANSMISSION OF PENICILLIN TO AMNIOTIC FLUID AND FETAL BLOOD IN THE HUMAN

J. H. E. WOLTZ AND H. A. ZINTEL

Am. J. Obst. &amp; Gynec., 50: 338-40, September, 1945

The present study was undertaken to determine the concentration of penicillin in the amniotic fluid and in the fetal blood after administration of the sodium salt of the drug to the mother by intramuscular and intravenous routes, and to attempt to form a preliminary estimate of the quantitative relationships of these concentrations at various times after injection.

Fifteen normal women were given sodium penicillin shortly before delivery, eleven by intramuscular injections of 25,000 units of penicillin in physiologic saline and four by intravenous drip method at the rate of 10,000 units of penicillin per hour. Penicillin was found to be present in the amniotic fluid following both of these methods of administrations. The concentrations were comparable to those of the maternal and fetal circulations. In those cases receiving intramuscular injections, the maximum concentrations in the fetal circulation and amniotic fluid were found 60 to 90 minutes following injection to the mother. The intravenous administration had been continued, in each case, for at least two hours before delivery, and in each case there was a significant amount of penicillin present in the cord blood and amniotic fluid. There was no evidence of penicillin toxicity to either mother or child in any of the cases.

The fact that adequate penicillin levels can be produced in the amniotic fluid as well as in the maternal and fetal circulations suggests the use of penicillin in the treatment of certain types of intrauterine infection as well as its prophylactic use following premature rupture of the membranes and during prolonged labor. The dosage, mode of administration and efficacy in these complications of pregnancy remain to be determined by future investigations. 3 references.

(On the basis of a small series of cases, perhaps 15 or 20, I have the impression that penicillin is of great value not only in the treatment of actual intrapartum infection but also as a prophylaxis against intrauterine infection in prolonged labor, in prolonged rupture of the membranes and in neglected cases which have been referred to the hospital after vaginal manipulation at home. On the assumption that penicillin passes through the placenta we have been in the habit of giving this drug also to patients with active gonorrhea, during the course of labor, in the belief that it will aid in the prevention of gonorrheal ophthalmia. The clear-cut report of Woltz and Zintel is hence most welcome in showing that penicillin actually does traverse the placenta and in very rapid fashion.—Ed.)

## BLOOD PRESSURE IN NORMAL PREGNANCY

GEORGE J. ANDROS

Am. J. Obst. &amp; Gynec., 50: 300-306, September, 1945

Antepartum blood pressure was studied in 300 cases of normal pregnancy. The series was unique in that all patients had had one or more pressure readings taken prior to the onset of pregnancy. In the 661 pre-pregnancy readings in the 300 cases there was an average "normal" blood pressure of 114.6/72.6 (pulse pressure 42). In comparing the average pre-pregnancy pressure (systolic, diastolic, and pulse) for the group as a whole with the average intra-pregnancy figures for the entire group calculated according to calendar month—or week—of pregnancy, no significant deviation in systolic pressure was noted at any time during gestation. Diastolic pressures were consistently lower than the "normal" in the first six and one-half months of pregnancy, but the drop was not marked. Deviations ranged from 2.64 to 4.15 mm. Hg. below the pre-pregnancy figure. There was no significant variation from pre-pregnancy diastolic pressure in the last two and one-half months of gestation. Average diastolic readings ranged from 68.43 at the third month to 75.66 at the last week before delivery. Average pulse pressure increased with the diastolic fall noted, varying between 46.20 at the third month down to 40.90 at the third week of the ninth month. Approximately two-thirds of the patients in the series exhibited some diastolic fall in the first trimester as a unit, and an identical number in the second trimester, but only an approximate one-half of the patients showed a diastolic pressure fall in both the first and second trimesters.

The conclusions reached were that systolic blood pressure does not vary at any time during normal pregnancy from the level for a normal and healthy young woman who is not pregnant and that there is evidence that diastolic blood pressure tends to be slightly lower in the first and second trimesters of normal pregnancy than in the normal nongravid state. On the basis of the study it would appear that any persistent, even though slight, increase in either systolic or diastolic pressure during pregnancy should be looked upon as potentially significant. 38 references. 4 tables.

## THE DISTRIBUTION OF CELL TYPES IN THE ANTERIOR HYPOPHYSIS DURING LATE PREGNANCY AND LACTATION

NEWTON B. EVERETT AND BURTON L. BAKER

Endocrinology, 37: 83-88, 1945

Within the last few years considerable evidence has accumulated from bioassays which shows that the lactogenic content of the anterior hypophysis increases markedly in mammals about the time of parturition. In some forms the

increase has been observed during pregnancy, whereas in others no notable increase occurs until the time of parturition or soon afterwards. In the present study differential cell counts of the hypophysis from pregnant and lactating rats show that at three days postpartum the acidophiles have increased by almost 100% above the number present in pregnant animals. This number decreases as lactation continues but does not revert to the pregnancy level. The increased number of acidophiles and their increased granulation is believed to be associated with the high lactogen content of the hypophysis. This increase of acidophiles was due to conversion of chromophobes and not from division of acidophiles. There is no significant weight change in the rat hypophysis during lactation as compared with pregnancy.

## THE INFLUENCE OF PREGNANT-MARES' SERUM ON THE PREGNANT RAT

A. ST.G. HUGGETT AND J. J. PRITCHARD

J. Physiol., 104: 5P, 1945

Investigations into the cause of fetal death in the rat following a single injection of follicle-stimulating hormone (F.S.H.) from pregnant-mares' serum and the subsequent changes in the placenta are reported. Fetal death was most easily produced by injection at the 10th day of pregnancy, with 50 I.U. the minimum effective dose. Lethal doses given at this time inhibit the penetration of allantoic blood vessels into the trophoblast. The decidual basalis becomes abnormally thick, due to the failure of normal involution. It is reduced in vascularity and shows large areas of coagulative necrosis. In spite of this decidual necrosis, absence of allantoic mesoderm and absence of fetus, the trophoblast usually survives, grows and differentiates in comparatively normal fashion. The authors conclude that the decidual changes are probably the ultimate cause of the fetal death. The only effect of F.S.H. given after the 12th day of pregnancy was to delay parturition beyond the normal 21 days. Retention after the 23rd day resulted in death of the fetus.

# MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

## THE EFFECT ON INFANT MORTALITY OF VITAMIN K ADMINISTERED DURING LABOR

ENITH L. POTTER

Am. J. Obst. & Gynec., 50: 235-47, September, 1945

This report presents the seemingly justified conclusion that no decrease in infant or fetal mortality can be expected to result from the routine administration of vitamin K to all women during labor.

The discovery of vitamin K with the realization that spontaneous bleeding often occurred in animals when the vitamin was absent from the diet has excited much interest in the possibility of decreasing the mortality of newborn infants due to bleeding. Many investigators have produced evidence that in the majority of infants, the prothrombin time is prolonged during the first week of life beyond the normal time for adults. Many also have claimed that the administration of vitamin K to the mother prior to delivery or to the infant after birth will usually prevent this prolongation, and that after prolongation has occurred, it may be returned to normal by the administration of vitamin K.

The evidence of numerous investigators seems to make this point conclusive; that is, that vitamin K will prevent a prolongation of prothrombin time and will return to normal one that is already prolonged. However, the important questions are whether or not hemorrhagic disease in infants is caused entirely by prothrombin deficiency and whether the incidence and mortality rate of hemorrhagic disease due to this deficiency are great enough to warrant the routine administration of vitamin K.

The opinion advanced by numerous investigators and based upon statistics from their experiments is that prothrombin deficiency alone cannot explain all cases of hemorrhagic disease in newborn infants. Many infants with excessively prolonged prothrombin time show no evidence of hemorrhage while others with relatively little prolongation bleed severely. Since almost all infants show some prolongation of prothrombin time during the first week, all who bleed from any cause would be expected to show some abnormality.

The optimistic prophecies which were made early in the study of vitamin K regarding a decrease in infant mortality due to hemorrhage by the routine administration of vitamin K have not materialized. The investigations of many, including Sanford, and Parks and Sweet indicate that in a carefully studied group of infants, anything which can be considered true hemorrhagic disease is extremely rare and that the incidence of hemorrhages which do appear in this age group is not modified by administration of vitamin K to the mother prior to delivery or to the infant after birth.

In order to evaluate further the claims of various investigators in regard to the value of vitamin K administration to reduce hemorrhagic neonatal mortality rates, a study of this subject was made at the Chicago Lying-in Hospital. For two years, vitamin K, in the form of 3.2 mg. Hykinone, was given to all patients on admission to the labor rooms. During the two following years administration of the vitamin was discontinued for a control study. The first group produced 6,560 infants weighing over 1,000 grams and the second group 6,630 infants. The total fetal and infant mortality rate for the first group was 29.8 and for the second group 25.8. Although the rate was higher for the group receiving vitamin K than for that not receiving it, there were no significant changes in the incidence of primiparity, premature delivery, mode of delivery or any other known factor. The mortality rates for liveborn infants are identical in the two series, as are also the number of infants who showed evidence of hemorrhage on postmortem examination.

In only two infants did the possibility of true hemorrhage exist and in neither of these was the diagnosis conclusive. In one of these cases, Hykinone was given to the mother before delivery; in the other it was administered to the infant. Both infants died.

It is the opinion of the Chicago Lying-in Hospital that the incidence of intracranial hemorrhage is directly related to the skill and judgment of the obstetrician.

From the evidence produced by the present study and by other investigators, it would seem that no decrease in infant or fetal mortality can be expected to result from the routine administration of vitamin K to all women during labor.

(This judicial clinical study by our leading student of neonatal pathology would seem to constitute well-nigh irrefutable evidence against the value of vitamin K administered in labor, and surely it has tempered the enthusiasm of many of us who, a few years ago, held high hopes for this vitamin as a means of lowering infant mortality. In view of Potter's findings, the curious thing about this whole matter is the large number of favorable reports on record. As an example, in the very same issue of the journal containing her article, appears another study, abstracted below, in which the authors reach just the opposite conclusion and recommend its use in labor; moreover, in the discussion which followed the presentation of these two papers at the Chicago Gynecological Society, another worker in the field, Augusta Weber reported as follows: In a study carried out at the Cook County Hospital by Webster and Fitzgerald (*Surg. Clin. N. A.* 23, 87, 1943), 5370 deliveries were observed, in 1720 of which the mother had received vitamin K in labor. Among 44 neonatal hemorrhages which occurred in the total series, 42 developed in the untreated mothers, whereas only 2 occurred in the cases in which vitamin K had been administered! The authors cannot believe that this dramatic difference was just an accident. Similarly, many other authors have endorsed the administration of vitamin K in labor on the basis of substantial series of cases. On the other hand, let it be noted, Parks and Sweet (*Am. J. Obstet. & Gynec.*, 44, 432, 1942) have obtained no effects on infant mortality from the use of the vitamin and hence agree with Potter.

How can it be that groups of sincere, forthright and presumably competent investigators should differ so decidedly on what would seem to be a rather simple problem, namely, the effect of the antenatal administration of vitamin K to the mother on stillbirth and neonatal mortality? There are several possible explanations.

1. Sampling errors, that is, the inadvertant inclusion, either in the vitamin K series or the untreated series, of a disproportionate number of cases which carry inherently an especial hazard to the baby, such as cases of premature labor. Potter believes that this error explains most of the favorable reports and certainly it must have played some rôle in the decided differences reported by Webster and Fitzgerald.

2. Dietary differences between the various series reported. For instance, if the previous dietary regime of Potter's series at the Chicago Lying-In Hospital was better than Webster and Fitzgerald's at the Cook County Hospital, the latter might be expected to be in more need of vitamin K. Against this supposition is the fact that the series of Parks and Sweet, who found no value in vitamin K, was made up of patients at the Gallinger Hospital in Washington who were very comparable, I believe, in social and economic status with the Cook County group.

3. Barbiturates. Both Webster and Fitzgerald, and Schmidt and Baba have found that barbiturates given the mother lower the prothrombin time of the new-born infant and that this hypoprothrombin state can be relieved by the administration of vitamin K antenatally. This may explain some of the discrepancies. Practically all of the cases reported by Hollman and his associates had received barbiturates for analgesia plus sodium pentothal for delivery.

In view of our own favorable results, the many concurring reports in the literature, the poor diets of many of our patients, and the possible barbiturate factor, we are continuing to use vitamin K despite the very convincing Potter report.—Ed.)

## AQUINONE DURING LABOR; ITS EFFECT ON THE PROTHROMBIN LEVEL OF THE NEWBORN INFANT

H. E. SCHMITZ AND GEORGE BABA

*Am. J. Obst. & Gynec.*, 50: 292-300, September, 1945

In this report, the conclusion is drawn that aquinone to laboring mothers has a prophylactic effect against physiologic or induced prothrombinemia.

A study of prothrombin levels in the newborn infant requires the consideration of such factors as maternal conditions prior to parturition and feeding schedules of the infants. Certain standards of technique should be adopted to reduce the elements of human error. In this study, a total of 231 unselected cases of newborn infants was investigated. These were classified according to whether the mother had received no medication during labor, analgesics only, analgesics and aquinone, or aquinone only. The data were analyzed to determine the minimum prothrombin level and the day by which this level was reached. The minimum level in most cases was reached by the third postnatal day. A precipitous drop by the first day was shown in those cases where no aquinone was used, while those with aquinone showed but a slight drop.

Other findings were as follows: labor analgesics in the form of certain barbiturates apparently exert prothrombinopenic effect on newborn infants. Icterus of varying degree was seen frequently in spite of the high or normal prothrombin level; some cases with low prothrombin levels manifested no icterus; aquinone administered intramuscularly in this series caused no discomforting symptoms.

Since the circumstances tending to produce fetal hemorrhage may be present as soon as labor begins, it follows that the administration of vitamin K should be sufficiently early to eliminate the role of prothrombinemia in the production of hemorrhage.

Dr. Augusta Webster discusses this report and that of Dr. Potter, who found that no demonstrable decrease in infant or fetal mortality could be expected to follow the routine administration of vitamin K to all women during labor. Dr. Webster's findings are similar to those presented in this report, including the observation that certain barbiturates lower the prothrombin level of the newborn infant, and that this hypoprothrombin state may be relieved by the administration of vitamin K to the mother during labor. 17 references.

### CAUDAL ANALGESIA IN OBSTETRICS WITH SPECIAL REFERENCE TO REPEATED SINGLE BLOCKS

B. J. HANLEY AND C. M. MALONE

*Am. J. Obst. & Gynec.*, 50: 306-11, September, 1945

The authors present the results which they obtained in a series of 1,925 cases using caudal block. In 152 of these cases, a technique for complete analgesia and delivery under repeated single caudal injections with  $\frac{1}{4}$  per cent tetracaine was employed.

In these latter cases, nembutal and aspirin were given during the first stages of labor and the first caudal block was given preferably after the head was engaged and the cervix dilated to at least 3 to 5 cm. The large majority of multiparas were carried through labor and delivery with a single injection. The average number of injections necessary for primiparas was 2.7.

In the entire series of 1,925 cases there were no maternal deaths from any cause and no fetal deaths attributable to this anesthesia. There were no infections of any kind.

Indications for caudal block are premature labor, heart disease and pulmonary disease. Its use is contraindicated where there are inadequate materials and personnel to combat every possible type of accident. It should not be used in patients with severe anemia, exhaustion, abruptio placentae, placenta previa, spinal deformity, or when disproportion is suspected.

Subdural and intravenous injection should be guarded against. Prophylaxis in the selection of cases will usually eliminate blood pressure drop, but when it does occur, elevation of the lower extremities and the use of ephedrine sulfate will usually combat it successfully. Absolute sterile technique is essential to prevent infection. The use of a 20 gauge flexible spinal needle, properly inserted, is recommended. There were no broken needles in this entire series of cases.

As compared with continuous caudal analgesia, advocated by Hingson and Edwards, caudal blocks do not require the constant and expensive attendance of

the trained anesthetist. The patient can move at will and be examined with ease. The chances for infection and broken needles are much less. The equipment is more manageable and one-sided analgesia is seldom seen.

Single caudal block has a definite place in obstetrics and is as safe or more so than other forms of analgesia. Correctly administered, it will give as good results as any other form of analgesia. The percentage of successful analgesia in these 1,925 cases was 96 per cent. A caudal block was considered successful if no additional anesthetic agents were required. The use of interrupted single caudal blocks for analgesia and delivery gives promise of effectiveness and safety for mother and child.

Caudal anesthesia in obstetrics should be limited to well-equipped institutions which have full-time resident or teaching staffs. 5 references.

## CONTINUOUS CAUDAL ANALGESIA IN OBSTETRICS ON TRIAL

R. E. NICODEMUS, L. F. RITMILLER AND J. L. LEDDEN

*Am. J. Obst. & Gynec.*, 50: 312-18, September, 1945

A comparative study is made of the results of continuous caudal analgesia and other forms of analgesia. Five-hundred patients, prior to the institution of caudal analgesia, were given sodium pentobarbital, if necessary a rectal oil ether mixture, and in all cases, inhalations of ethylene or nitrous oxide at the actual time of delivery and repair. Another 500 subsequent cases were given continuous caudal analgesia.

Analysis of the results from these two types of analgesia shows that where caudal analgesia is used, the labors are usually longer. Uterine contractions are of less intensity and the expulsive force of the abdominal musculature is lost. Occiput posterior positions rotate less often and operative deliveries are increased. In contrast, the advantages of this technique are a lower incidence of stillbirths, easier and safer breech deliveries, a lower maternal morbidity, diminished blood loss with delivery, less permanent injury to the birth canal and a pleasant, co-operative happy patient. The postpartum response of the patient under caudal analgesia is superior to that of the patient receiving other analgesia.

Such dangers as needle breakage, infection, penetration of the subarachnoid space, etc., need to be controlled by careful thought, judgment and attendance on the part of the doctor.

Dr. Robert A. Hingson believes that continuous caudal analgesia should be put on trial by all obstetricians who still manage women in pain throughout labor and delivery. He confirms the fact that it does prolong labor and states that its application should be guided by this consideration. Prolonged caudal blocks above the segmental levels of thoracic 8 impair the forces of labor.

Dr. Thaddeus L. Montgomery writes that the crux of the situation seems to lie in the problem of how far one should go with any method of anesthesia which inhibits the natural powers of labor. However, the lack of anoxemia in the baby

and the freedom from inhalation accidents to the mother in caudal and spinal anesthesia, represent quite a step forward.

Dr. W. Royce Hodges reports that most of his disappointments in caudal analgesia were due to personal failure in technique. He advises against too early administration of this type of anesthesia and against allowing the analgesia to necessitate operative deliveries.

## FIVE YEARS' EXPERIENCE WITH CAUDAL ANESTHESIA IN PRIVATE OBSTETRIC PRACTICE

ARTHUR BAPTISTI, JR.

*Am. J. Obst. & Gynec.*, 50: 180-183, 1945

This is a report of the author's experience in 320 cases with a procedure for terminal caudal aesthesia which can be employed without trained assistance. The procedure was completely satisfactory in 316 cases, with no maternal or fetal complications; in two instances administration was abandoned because the caudal space could not be penetrated, and in two supplementary anesthesia was found necessary. The equipment includes one each of the following: small towel; 3-inch, 19-gauge spinal puncture needle; small hypodermic needle; 10-cc. syringe; 150-cc. Pyrex basin; ampule containing 5 cc. of 20 per cent metycaine with file for opening; and several gauze sponges. With the patient in hard labor and lying on her side with knees flexed, an area of skin overlying the sacral hiatus is cleaned with iodine followed by alcohol. The metycaine is diluted with 60 cc. of sterile normal saline solution. Several cc. of this solution are then allowed to infiltrate the skin and subcutaneous tissues overlying the hiatus. The patient is then placed in the knee-elbow position and three injections of 10-cc. amounts of the metycaine solution are given through the hiatus into the sacral canal at intervals of several minutes. The patient may be placed on her left side after the first injection. Between injections the radial artery is palpated and the pulse checked. In the event of weakening pulse or other indication of accident from the previous injection, the following one is deferred. After the third injection the patient is placed on her back. Anesthesia lasts approximately one hour.

## THE USE OF AN ERGOVINE-LIKE OXYTOCIC (METHERGINE) A PRELIMINARY REPORT

JOHN C. BROUGHER

*West. J. Surg., Obst. & Gynec.*, 53: 276-277, 1945

In the author's series of 288 consecutive deliveries Methergine was employed intravenously in 271 cases and intramuscularly in 7 cases. The procedure was

as follows. One cc., containing 0.2 mg. of d-lysergic acid d-l-hydroxybutylamide 2, was given when the fetal shoulder appeared under the pubic arch. By inserting the needle in the cubital vein at the time the episiotomy was made it was possible to expel the contents of the syringe at the correct time. One tablet of Methergine, containing 0.25 mg. of d-lysergic acid d-l-hydroxybutylamide 2, was given orally three times daily for two days postpartum.

The smallest loss of blood, exclusive of episiotomy bleeding, in this series was 10 cc. and the maximum 300 cc. Ninety-one percent of the patients lost less than 100 cc. and 50 per cent lost 50 cc. or less, exclusive of episiotomy. Bandl's ring with retention of the placenta was observed in three patients. In these and others in which some difficulty was noted in expelling the placenta, there had been difficulty and delay in entering the vein. The Brandt method of expressing the placenta was found advantageous in the early removal of the placenta and lessened the amount of blood loss to a considerable degree below that which occurs when the placenta is allowed to remain for several hours for spontaneous expulsion.

When these results were compared with those obtained in 288 deliveries in which Ergotrate (ergonovine) was given intravenously when the shoulder appeared, no great differences were found with reference to blood loss, morbidity, mortality or retention of placenta. However, the uterus remained contracted longer when Methergine was used rather than Ergotrate or any of the other ergot alkaloids. Methergine contracts the uterus within 20 to 30 seconds after intravenous administration and the action continues six to eight hours, after which Methergine tablets are administered postpartum as mentioned above.

## CLINICAL EXPERIENCE WITH A NEW SYNTHETIC ERGONOVINE-LIKE SUBSTANCE

JOHN E. TRITSCH AND EDWARD SCHNEIDER

*Am. J. Obst. & Gynec.*, 50: 434-38, October, 1945

The authors present a preliminary report of their experience with Methergine in 200 cases of postpartum bleeding. Methergine is a synthetized derivative of ergonovine.

In 100 cases, 1 cc. of Methergine, containing 0.2 mg. per cubic centimeter, was given intramuscularly immediately following delivery of the placenta. In the other 100 cases, the same preparation and dose was given intravenously immediately following birth of the child and before the placenta was delivered. In both groups, the blood was measured as preplacental, placental, and for thirty minutes after birth of the placenta. No deductions have been made for bleeding from lacerations or episiotomies in the routine case.

In the cases handled by the intramuscular method, a modified Crede maneuver was used to deliver the placenta. In the cases handled by the intravenous method, the placenta was delivered in the following manner: The umbilical cord

was clamped close to the vulva. The uterus was palpated to insure a firm contraction. The clamp at the vulva was then held firmly in one hand while the fingertips of the other hand were inserted abdominally between the fundus and the symphysis pubis. Upon elevation of the fundus toward the sternum, failure of the cord to retract into the vagina was taken as evidence of separation of the placenta and continued elevation of the fundus associated with minimal traction on the cord resulted in delivery of the placenta. Where the cord retracted into the vagina, the placenta was assumed to be attached or incarcerated, and no attempt was made to deliver the placenta until later repetition of the maneuver revealed its freedom. In all cases, the blood loss was measured accurately.

In both the intravenous and intramuscular groups there were 30 primigravidas and 70 multigravidas.

The average blood loss with the intravenous technique was 113.24 cc. The average blood loss for the intramuscular group was 168.07 cc. In the intravenous group, the primigravidas averaged 116.03 cc., while the multigravidas averaged 112.05 cc. In the intramuscular group, the primigravidas averaged 173.0 cc., while the multigravidas averaged 165.96 cc.

The largest blood loss occurred in one case of the group receiving Methergine intramuscularly. However, in this instance, other factors which could not be controlled by Methergine or any oxytocic were felt to be responsible. The smallest blood loss occurred in the group receiving Methergine intravenously; in many of these cases the blood loss was so slight that it could not be measured.

The third stage averaged 7.68 minutes in the intravenous group and 10.38 minutes in the intramuscular group. No attempt was made to deliver the placenta as soon as it was separated. In most cases, the baby was attended and then the third stage was terminated. In spite of this, the third stage in both groups of cases was of shorter duration than the average time quoted as normal in textbooks.

Manual removal of the placenta was required three times in the intravenous group and not at all in the intramuscular group.

In summary, Methergine appeared to reduce postpartum blood loss by both methods of administration as compared to other available statistics. When given intravenously immediately after the birth of the infant, the drug produced definitely less blood loss than when given intramuscularly immediately following placental delivery. By the intravenous route, immediately following delivery of the child, the placental delivery is accelerated by about three minutes. Incarceration occurred in the intravenous group in 3 per cent of the cases, but placental removal was easily accomplished under general anesthesia.

One table; two figures. Twenty references.

## PATHOLOGY OF PREGNANCY

### ESTROGEN-PROGESTERONE THERAPY: A NEW APPROACH IN THE TREATMENT OF HABITUAL ABORTION

NORRIS W. VAUX AND A. E. RAKOFF

Am. J. Obst. & Gynec., 50: 353-366, 1945

This intensive study of habitual abortion presents evidence to show that the condition is best treated by supplementing progesterone with estrogen therapy. In studies which the authors have made over a number of years on the blood and urine hormonal levels of normal and abnormal pregnancies they have been impressed not only by the high percentage of habitual aborters who exhibit low pregnanediol titers, but even more by the frequency which these are associated with diminished blood and urine estrogen levels. Since both of these hormones are believed to be made by the corpus luteum during early pregnancy, these findings would support the diagnosis of premature failure of this structure; but since this same type of double deficiency was often noted by the authors after the first trimester, they were led to believe that the placenta can be equally responsible for the failure to produce estrogen and progesterone. These findings encouraged the authors during the past three years to treat their habitual aborters with combined estrogen-progesterone therapy.

The present study was made on a group of twenty-four women in whom the previous two or more pregnancies had terminated in abortions. These patients had gone through a total of eighty previous pregnancies from which there had resulted only seven (9 per cent) full-term living infants, despite various types of treatment in many of the pregnancies. There were fifty-two instances of termination of pregnancy in the first trimester, eighteen in the second, and one case of a premature baby which lived only a few minutes. Twenty of these twenty-four had no living babies. No patients were included in the study who had pelvic tumors or other abnormalities which might conduce to abortion.

Hormone assays consisting of urine pregnanediol determinations, serum estrogens and serum gonadotrophins were made early in pregnancy in nineteen cases. In almost all of the cases one or more additional assays were made and in three monthly assays were done. On the initial assay 95 per cent of the cases showed normal serum gonadotrophin. Seventy-nine per cent had diminished serum estrogens and 83 per cent had diminished pregnanediol titers. In thirteen of the nineteen cases studied, both estrogen and pregnanediol were diminished. These findings indicate a deficiency of the corpus luteum during the early weeks of gestation and an inadequacy of the placenta to take over its functions.

During the present pregnancy all patients were treated by the injection of progesterone, 10 mg., and alpha-estradiol benzoate, 10,000 rat units, given two or three times weekly. Treatment was started by the fourth week of gestation

in six cases and by the tenth week in the remainder and was generally continued to the period of viability or later.

There was a total of eighteen live births of which sixteen survived as living healthy infants making a fetal salvage of 67 per cent. There were fifteen full-term live births (with one neonatal death due to congenital abnormalities), three premature live births of which two survived, and six abortions of which two occurred in the second trimester and four in the first. Perhaps the most striking case in the series was a patient who had had seven spontaneous abortions at approximately eight weeks of gestation in each instance. During six of these pregnancies she had received progesterone which in the last two pregnancies had been given in a dosage of 20 mg. a week. She had also received vitamin E in most of these pregnancies and in three of them received thyroid extract despite the fact that the basal metabolic rate was always within normal limits. In her eighth pregnancy she was treated with the estrogen-progesterone regime described above and gave birth to a normal, healthy infant at term; moreover, at the time the paper was written she was again pregnant, was on the same therapy and had reached five and a half months.

The authors outline the rationale for the addition of estrogen to progesterone in the treatment of habitual abortion as follows: 1. Progesterone and estrogen are believed to come from the same sources throughout gestation, and their concentration throughout gestation roughly parallel each other. 2. It is logical to assume that a deficiency in progesterone would be accompanied by a deficiency in estrogen. 3. In the authors' experience such double deficiencies of estrogen and progesterone frequently occur in abortion patients, often appearing early in the gestation and persisting in many cases throughout the period of gestation. 4. There are good reasons to believe that estrogen and progesterone influence the normal reactions of each other upon the uterus and are involved in the normal metabolism of each other.

## THERAPY IN HABITUAL ABORTION

C. H. INGRAM, JR.

Am. J. Obst. & Gynec., 50: 154-159, 1945

Six cases of habitual abortion in which treatment with a combination of mixed tocopherols (Tocopherex) and oral pregnenolone (Pranone) has proved completely successful are reported. A total of 16 previous pregnancies in this series of women had yielded only two living babies. Four of the patients had had treatment in at least one prior successful pregnancy. Four were given desiccated thyroid in addition to the preparations mentioned above. All the patients were given one capsule (3 drops) of the mixed tocopherols three times daily as soon as the first period was missed, two capsules a dose for three days before the next

period was due, three capsules a dose during the days of expected flow, two-capsule doses for another three days, and then one-capsule doses until time for the next period, except in the event of either cramps or bleeding when the dose was promptly increased to three capsules. This regime was continued at least until definite fetal movements were felt by the patient. Oral pregnenolone or Pranone was also given in 5-mg. doses on the first three days of each expected period prior to quickening and on evidence of threatened abortion. The patients were cautioned against undue exertion and advised to take extra rest at the time of expected periods. Intercourse was prohibited. All the patients were delivered of normal infants, one 18 days prior to the expected date and the others at dates varying from 5 to 17 days later than expected. It is pointed out that success of this treatment depends upon starting it before the onset of any signs of threatened abortion, preferably as soon as a pregnancy is attempted, or as soon as the first period is missed. It may be used in conjunction with other indicated corrective measures, but does not replace them. Whether or not it has beneficial effects upon any future pregnancies was not ascertained.

## THE STATUS OF ABORTION IN SOVIET RUSSIA

ANNA KLEEGMAN DANIELS

Med. Woman's J., 52: 21-7, 1945

During the 18 years (1918-36) that the free legal abortion policy was in effect in Soviet Russia maternal death rates following abortion were lower than those from childbirth; moreover, septic infection and perforation of the uterus were not common. However, serious pelvic disorders, decreased fertility, ectopic pregnancy, tendency to spontaneous miscarriage, prolonged labor, endocrine dyscrasia and derangement in normal sexual response were seen with increasing frequency as sequelae, even though the previous abortions had been done under aseptic conditions in the abortaria. It was for this reason that the law of June 27, 1936, making abortions legal only under special medical conditions, was passed. The medical indications for abortion include severe and chronic organic disturbance of the heart and blood vessels, chronic forms of inflamed, degenerative, sclerotic affections of the kidneys, bilateral nephrolithiasis, various forms of tuberculosis, chronic parenchymatous affection of the liver, and Basedow's disease. Permission to abort must be obtained from the medical commissions of the Health Commissariat of the various union republics. Abortions may be performed only at hospitals or maternity homes. There is a charge (the amount of which is decided by the particular commissariat for health) and, when permission is granted, the medical institution to which the woman is sent does *not* have the right to refuse to perform the operation. On July 8, 1944, a new law for the care of mothers and infants was passed. This law provides for increased vacations for pregnant and nursing mothers; financial assistance before the birth

of the third and subsequent children; single grants at birth and a monthly allowance between the child's first and fifth birthdays; taxes on single persons and childless couples (6 per cent of income) and those with one or two children (1 per cent and 0.5 per cent, respectively); and protection of the unmarried mother.

## ECTOPIC PREGNANCY

EDWARD ALLEN

Clinics, J. B. Lippincott Co., 4: 648, October, 1945

Most of the important contributions in the study of ectopic gestation have placed great stress on the evidence of pelvic inflammation found at the time of operation as a probable cause of this condition. The average reported incidence is more than 40% of all cases. The author has not found this to be true in his series and he seriously questions the place accorded to it in the etiologic array. His reasons for these doubts are based on the following observations and deductions: (1) The mobility of the affected tube in early ectopic pregnancy which allows simple vaginal removal. (2) The absence of external evidence of firm adhesions to the serosal coat of the tube. (3) The normalcy of the tubal mucous membrane at some distance from the site of implantation. (4) The lack of evidence either clinically or microscopically of chronic inflammation in the affected area. (5) Elevations of temperature in ectopic pregnancy usually subside promptly when the hemorrhages into the peritoneal cavity and tubal wall are controlled. If chronic inflammations were chronically present we should reasonably expect a more continued febrile postoperative course; especially in the presence of free blood in the surrounding tissues. (6) Much of the fixation and suggested evidence of pelvic inflammation in a late ectopic pregnancy can readily be explained by progressive trophoblastic reaction and nature's attempt at boiling off and controlling repeated hemorrhage. (7) Ectopic pregnancy is not as common in the colored patients as in the white; yet the incidence of pelvic infection is considerably higher in the negro. (8) The occurrence of tubal pregnancy in the opposite tube of patients in whom we have removed a previous ectopic pregnancy and noted at that time an apparently normal opposite tube. (9) Our observation of a patient who had no history or gross evidence of a pelvic infection but had given birth to a spina bifida baby from one husband and from whom we were able to remove through the vagina two ectopic pregnancies at different times by the second husband; which fact suggests a primary defect in germ plasma.

Practically all deaths from ectopic pregnancies occur in those patients in whom delay has permitted gross complications to arise or in those in whom complicating conditions overshadow the symptomatology or palpatory findings

of an abnormally situated pregnancy. A concentrated effort on the part of physicians in teaching patients and students alike concerning the great importance of irregular vaginal bleeding would do much to overcome many of these serious delays and mistakes. Women are not alarmed about bleeding from the vagina unless it is greater in quantity than their monthly loss. Vaginal bleeding in ectopic pregnancy is usually not profuse. Vaginal bleeding from extrauterine pregnancy frequently occurs at or near the time of the next expected menstrual period and goes unnoticed. Since women are so notoriously inaccurate concerning their menstrual function, they are unaware that the bleeding is abnormal in character. Any patient who complains of irregular bleeding is to be suspected of having pregnancy or malignancy until proven otherwise. The shorter the period of amenorrhea preceding the onset of bleeding, the more apt is the implantation to be extra- rather than intrauterine. The more profuse the bleeding encountered, the more apt it is to be caused by an intrauterine rather than an ectopic pregnancy.

A carefully taken history in ectopic pregnancy is by far the most important diagnostic aid in our armamentarium. Many of the vicious delays in beginning treatment are based on an inaccurately taken or evaluated history of the case. Added to this is the increasing present day tendency in all medicine to place too much dependence on laboratory results. Many patients with ectopic pregnancy have succumbed because the pregnancy test of the urine was negative, the hemoglobin was normal, the leucocyte count too high, the pulse too slow or the systolic blood pressure had not as yet taken its spectacular drop preceding death. The author's experience has coincided with that reported in the literature, that the pregnancy urine test both by rabbit and frog has been negative in approximately one third of extra-uterine pregnancies.

The author is convinced that the routine use of posterior colpotomy in all cases of extra-uterine pregnancy except those that are gravely ill will materially reduce the serious delays in diagnosis and treatment as well as increase the number of cases in which vaginal removal of the affected tube or ovary can be undertaken. In the author's series of cases the period of hospitalization, post-operative discomforts and maternal risk have been materially decreased by removal through the vagina. To this may be added those patients in whom the early diagnosis of tubal pregnancy was made by colpotomy although the pregnancy was later removed by incision through the abdomen. An analysis of the operative records of patients operated upon by the gynecologic staff of the Presbyterian Hospital, Chicago, between 1919 and 1944, reveals the progressive tendency to approach extra-uterine pregnancy through the cul-de-sac both as a diagnostic and therapeutic measure. Thus, before 1940, 35 of 159 cases were handled by posterior colpotomy while between 1940 and 1944 30 of 64 cases were so treated.

THE CONSERVATIVE MANAGEMENT OF SOME VARIETIES OF  
PLACENTA PREVIA

HERMAN W. JOHNSON

Am. J. Obst. &amp; Gynec., 50: 248-254, September, 1945

The main purpose of this paper is to make a protest against continuously inculcating into the minds of medical students and of practicing physicians the impression that a case of placenta previa can end fatally as a direct result of the first blood loss, or even of any subsequent bout of bleeding, when no attempt at delivery has been made. It is the author's opinion that the obstetrician should not approach or behold a case of placenta previa with this unwarranted fear in his mind, since such an attitude might cause him to resort to measures in treatment which might be too drastic or untimely. Furthermore, most authorities importune the physician to terminate the pregnancy as soon as the diagnosis of placenta previa has been made. This appears unwarranted. There would seem to be no good reason for sacrificing the life of a fetus merely because its placenta happened to be implanted over or near the cervical os. More particularly is this true when the claimed serious threat to the life of the mother is still unproved. The high fetal mortality in placenta previa cannot be reduced unless the pregnancy is allowed to proceed into the period of viability and until the practice of using the body of the fetus as a mechanical plug is discontinued.

In recommending a waiting policy in certain cases of placenta previa in which the fetus is premature the author does not mean to suggest that every patient with a nonviable fetus and placenta previa should be carried along indefinitely. The tendency has always been to interfere at too early a stage in pregnancy. The author's contention, however, is that it is safe for both mother and child, provided the mother's blood picture is followed carefully. This must be the criterion for interruption of the pregnancy before the fetus has reached easy viability, and not an alarming history derived from a lay estimate of the amount of blood lost. Procrastination must end when the total blood loss has produced a secondary anemia of such severity that further bleeding would endanger the life of the mother.

All cases of suspected placenta previa should be hospitalized for purposes of accurate diagnosis and for close observation of a developing anemia. Hospital rest may also decrease the bleeding episodes while awaiting good viability of the fetus. If, for economic reasons, this is impractical, the patient should be returned to the hospital for careful blood study after each bleeding spell of any consequence.

It is essential to proper treatment that all means at our command be used for the purpose of making a correct diagnosis. The assumption that vaginal bleeding at term or during the last trimester is due to placenta previa is grossly erroneous. Indeed, it should be constantly borne in mind that only about thirty-three per cent of such cases of bleeding are actually due to placenta previa.

Two methods of localizing the placenta are available, namely, X-ray visualization and manual examination. All cases of suspected placenta previa should have the benefit of both. It is the author's opinion that a sterile vaginal examination is essential for accurate diagnosis. It should be done in all suspected cases of placenta previa whether there is bleeding or not. Rectal examinations are contraindicated, as zeal for information may cause too much trauma. Naturally the examination should be done with due consideration for the exigencies of the case and with extra precaution against infection.

When the pregnancy is terminated either with the onset of labor or by prearrangement, it will, for purposes of treatment, fall into one of two groups, namely, those best delivered by Cesarean section and those best delivered per vaginam. The first group includes all cases of central placenta previa and probably, in the interest of the baby, practically all previas in primiparas. This arrangement leaves for the second group those cases of partialis and marginalis occurring in multiparas. In the first group it is imperative only that the operator make sure that the operation is done at the safe time, i.e., that the blood pressure be sufficiently high to withstand the sudden additional blood loss following separation of the placenta. Inasmuch as the incidence of placenta previa increases with multiparity, the second group will include a large number of cases. It is for this group that the writer strongly advocates the ultraconservative treatment as opposed to bagging, version, scalp traction, etc. It is helpful for one using it to have the earnest and positive conviction that untraumatized and unhurried previas do not bleed to death. Otherwise, a puddle of blood may cause one to change the treatment at the wrong time and with dire consequences.

The patient is taken to the delivery room and prepared and draped for delivery. With the utmost care the middle finger of the left hand seeks a place near the edge of the placenta where the membranes alone separate the finger from the presenting fetal pole. Using the finger as a director, uterine dressing forceps are passed to contact the membranes. Then, instead of puncturing them, the tips are used to bite a perforation. The forceps are inserted further and opened in order to produce a large rent. This allows the amniotic fluid to escape freely. The patient is returned to her room. As labor progresses, the presenting pole aids the dilatation and acts as a natural tampon. The labor is then watched with frequent checking of the blood loss, blood pressure, and fetal heart. Following delivery of the infant the placenta should be allowed to separate naturally.

The author reports seventy-nine cases managed as described above with one maternal death and a fetal mortality of 22.2 per cent.

(See Editorial Note following next abstract.—Ed.)

## PLACENTA PRAEVIA—A STUDY OF 174 CASES

C. H. G. MACAFEE

Journ. Obstet. and Gynaecol. Brit. Emp., 52: 4, August, 1945

In the treatment of 174 cases of placenta previa between 1937 and 1944, the author had two main objectives: (1) The reduction of fetal mortality without unfavorably affecting the maternal death-rate. (2) The preservation of an open mind with regard to the appropriate treatment of a particular case, i.e., that each case should be treated, not necessarily on any "standard" lines, but in accordance with the conditions found.

A vaginal examination should be made in all cases of suspected placenta previa, but the time at which this examination is made must be carefully chosen. In the later years of the period under review the attitude adopted has been that placenta previa is not an obstetrical emergency which must necessarily be dealt with at the first hemorrhage, and that a vaginal examination must not be made until the appropriate subsequent treatment can be carried out.

One of the main causes of fetal mortality in placenta previa is prematurity. This mortality can be reduced only by carrying on the pregnancy to as near term as possible. Several patients in this series have remained in the hospital for weeks (one for fourteen weeks) and have had up to nine hemorrhages before any vaginal examination or manipulative treatment was carried out.

The following argument can be advanced in favor of this attitude: (1) The rarity of severe initial hemorrhage in cases of placenta previa. In the author's experience this complication rarely occurs apart from vaginal manipulation. (2) A certain number of cases have a sharp but not severe initial hemorrhage at 30 to 34 weeks without any further loss. (3) There are a large number of cases of antepartum hemorrhage with a history apparently typical of placenta previa when the hemorrhage is either not due to a low-lying placenta or due to a degree of placenta previa which can be safely treated by methods other than Cesarean section.

In this series, 81 cases or 47.6% were treated at the time of the initial hemorrhage. In the earlier years it was difficult to get rid of the dictum "There is no expectant plan of treatment for placenta previa" but with increasing experience the proportion of those patients who were treated immediately following the first hemorrhage gradually diminished.

From the experience gained over the last eight years the author feels that there is a very definite place for expectant treatment, even after the patient has had several small hemorrhages.

Among those patients treated expectantly there has been nothing to confirm the belief that recurrent hemorrhages tend to lead up to a catastrophic hemorrhage. Many patients have been under observation for weeks during which numerous small hemorrhages have occurred without causing any serious anxiety. Naturally, if a hemorrhage should occur while a patient is under observation and

approaching term, that is thirty-eight weeks, treatment is carried out at that stage to avoid the risk of further loss of blood. This attitude has meant that the infant's chance of survival is much enhanced. By way of supporting this statement, the author points out that in his last 47 cases, treated in large measure expectantly, the average weight of the babies was six pounds, twelve ounces; whereas the average weight of the first 47 cases in the series in which treatment was generally instituted at the time of the initial hemorrhage, was only five pounds, two ounces. Moreover, the fetal mortality in the 47 early cases was 47 per cent, whereas in the last 47 cases it was only 6 per cent.

In connection with the terminology of placenta previa the author deprecates the use of the terms "lateral" and "marginal" which are not used consistently by medical authors. He prefers the classification recommended by Professor F. J. Browne, as follows: Type 1, in which the placenta encroaches upon the region of the internal os, so that it can be reached by the physician on digital exploration about the cervix, but is not actually in contact with the os. Type 2, in which just the edge of the placenta reaches the edge of the internal os. Type 3, in which the placenta partially covers the internal os. Type 4, in which the placenta completely covers the internal os. For the treatment of cases of Type 4 and most cases of Type 3 the author prefers Cesarean section; some cases of Type 2 are treated by Cesarean section, others by artificial rupture of the membranes, while in Type 1 artificial rupture of the membranes is considered by the author as usually sufficient to control the hemorrhage. In general, the author prefers low cervical Cesarean section and of the 68 abdominal deliveries performed in this series 47 were of the lower segment type and 21 were classical.

In the series of 174 cases there was but one maternal death and a gross fetal mortality of 23.5%.

(The two papers abstracted above, the former by Johnson of Houston, Texas, and the latter by Macafee of Belfast, Ireland, are progressive contributions to clinical obstetrics of the first order and will make obstetricians everywhere ponder the wisdom of their past management of placenta previa. There has heretofore been rather general agreement that placenta previa demands prompt delivery and that temporizing for any purpose is rarely if ever indicated. Johnson and Macafee, working independently and indeed on opposite sides of the globe, reach conclusions on this subject which are alike as two peas and which are diametrically opposed to this old teaching. They not only show that a waiting policy is justifiable in many cases of placenta previa because it improves the fetal prognosis markedly, but they also demonstrate very convincingly that such a program can be carried out with complete safety to the mother provided certain precautions are exercised.

Both papers are based on the contention that the initial hemorrhage in placenta previa is rarely, if ever, fatal in the absence of vaginal manipulation, and that subsequent hemorrhages are rarely, if ever, fatal in the absence of vaginal manipulation provided the hemoglobin is normal at the onset of the hemorrhage. In a recent analysis of 304 cases of placenta previa at the Johns Hopkins Hospital, a particular effort was made to investigate the validity of the above contentions with the following result: in no single instance was an initial hemorrhage fatal except after extensive vaginal manipulation; in no single instance was a subsequent hemorrhage fatal except after vaginal manipulation; only one patient died undelivered (in 1920), a woman who refused medical attention, had four hemorrhages a week or so apart and fainted following the last; even in this neglected, exsanguinated woman, who received no transfusion, death did not occur until intra-cervical manipulation precipitated further bleeding and shock.

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forceps; cesarean section) was 31.1 per cent. The rate for the deliveries by cesarean section was 18.2 per cent.

The best results from vaginal delivery were obtained in those cases in which the bleeding could be controlled by simple rupture of the membranes and the fetus delivered either spontaneously, by forceps, or by breech extraction. Each patient should be evaluated as to the manner of delivery.

Following cesarean section there was a slight increase in the morbidity rate and an increase in the number of days the patient remained in the hospital, but the fetal mortality was greatly improved and the delivery simplified by this procedure. The type of cesarean section and the choice of the anesthesia seem of little importance. Further study toward the prevention of phlebitis is important.

Nine tables.

## RUPTURE OF THE UTERUS

J. H. MORRISON AND L. H. DOUGLASS

*Am. J. Obst. & Gynec.*, 50: 330-35, September, 1945

The authors present forty-five cases of rupture of the pregnant uterus with self-explanatory tables and a minimum of comment.

The greatest cause of rupture and mortality was previous classical section; the second greatest cause was version and extraction. In this series, there were 17 instances of rupture following previous section, four of these having been low cervical operations. In every instance the original incision had been longitudinal. Since the longitudinal approach is routine in the authors' clinic, this is not surprising and should not be construed to mean that the transverse incision in the lower segment is safer. Indeed, should rupture occur in a subsequent pregnancy, the longitudinal tear might be preferred since it shows less tendency to extend and involve large blood vessels, and lends itself more easily to repair.

Other important causative factors are implantation of the placenta under a section scar and multiparity. If four or more pregnancies have gone to term and a condition arises requiring section, it would appear to be conservative obstetrics to sterilize such a patient.

Complete ruptures are more often fatal than incomplete. Ruptures occurring at home carry twice as much risk as those occurring in the hospital where prompt treatment can be instituted. Delivery from above is preferable.

In regard to treatment, excellent results were obtained in those cases in which the uterus was repaired and allowed to remain in the abdomen, sterilization being done at the time of operation.

The causes of rupture and mortality emphasize the need for early diagnosis and laparotomy. Diagnosis was made correctly in only one-half of these cases

The recommendations in these two papers will do much good provided they do not result in callousness to hemorrhage. Certainly, they should dispel forever the old notion that a patient with placenta previa who bleeds substantially at home should be packed vaginally before being transported to a hospital. This procedure is of no value save to conceal bleeding. The observations of Johnson and Macafee now show that it is unnecessary. The findings of these authors also demonstrate that in every case of placenta previa there is ample time to provide for blood transfusion and to make careful preparation for whatever type of treatment may seem best.

But how shall we manage a case of pregnancy at thirty weeks or so, in which a single, moderate hemorrhage occurs, stops completely and vaginal examination shows placenta previa? Shall we effect delivery promptly, as generally taught, or attempt to carry the patient to a time when the baby has a better outlook? Provided the patient is in the hands of an obstetrician of seasoned judgment (and no case of placenta previa should be in other hands), provided she is in a modern hospital with an alert staff and a good blood bank, and provided the patient's blood loss and hemoglobin are vigilantly followed, it is apparent that much greater latitude is permissible in carrying these patients to the period of viability than has heretofore been realized.—Ed.)

## MANAGEMENT OF PLACENTA PREVIA: A TWELVE-YEAR STUDY

HERVEY C. WILLIAMSON AND ARTHUR V. GREELEY

*Am. J. Obst. & Gynec.*, 50: 398-406, October, 1945

The purpose of the study is to analyze the results of the present methods of treatment of placenta previa, and to indicate by what means further improvement of the treatment may be achieved. The use of cesarean section for placenta previa has been demonstrated to be one of the most important factors in this improvement. Prior to the use of this method a maternal mortality rate of 10 per cent and fetal mortality from 50 to 60 per cent were considered satisfactory. These figures have been greatly reduced by the judicious use of cesarean section. Blood transfusion has also aided in lowering the maternal mortality rate. Delay in operative treatment, after careful study of bleeding patients who probably have placenta previa, is wise.

The report is based on the study of 162 cases of placenta previa, in which the diagnosis was made either by vaginal examination prior to delivery, or by noting the placental location at the time of cesarean section. In the 162 cases in the series the types of placenta previa were: marginal 60; partial 30; central 65; unclassified 7. Seven patients developed phlebotic phenomena, an incidence of 4.3 per cent. There were 5 maternal deaths, making a mortality rate of 3.1 per cent. Among the patients delivered by cesarean section, 77 in number, there was one death, making a mortality rate of 1.3 per cent in this type of delivery. One patient in the series died before delivery, so the death rate for the vaginal delivery group was three in 84, or 3.6 per cent. The total fetal mortality rate for the 161 deliveries of various types (bag with spontaneous breech or forceps; bag with version and extraction; version and extraction alone; spontaneous breech or

Delivery should not be attempted until convulsions are controlled and the patient rational for one or two days. Many patients go into labor spontaneously during that period. If not, medical induction or rupturing of the membranes can be carried out. If the patient is a primipara near term, with a closed, thick cervix, a cesarean section can be considered and performed rather safely, provided the eclamptic state has been controlled for a time.

Since the report on the cases of 1942, the hospital has continued to use this method of treatment and has found it very successful. They had one patient in 1943 who did not respond and died.

One table.

## INFECTIONS OF VAGINA DURING PREGNANCY

J. BERNARD BERNSTEIN

Clinics, J. B. Lippincott Company, 4: 771-795, October, 1945

In the Department of Obstetrics of the Jefferson Medical College Hospital, it was found that approximately seven per cent of the patients admitted to the Outpatient Maternity Department had gonorrhea. When statistics are drawn from all classes of society it would seem that an incidence of about two per cent would be more nearly correct and the author considers that the true incidence lies between two and four per cent. In general, during pregnancy the disease remains confined to the lower genital tract and it appears quite evident that pregnancy acts as a barrier against an ascending infection. Accordingly, the pregnancy is not affected but naturally such an individual may transmit the disease in the usual manner. Most important are the consequences of gonorrheal infection that may occur following abortion or during the puerperium, especially ophthalmia in the neonatum period.

Cultural methods of identifying the gonococcus have been shown to be much superior to reliance on smears alone. Lankford, in a study of 3,060 cervical specimens with a total of 485 positive, reports that nearly three times as many positives were obtained by culture as by smear. In the treatment of acute gonorrhea in pregnancy the author has used both penicillin and the sulfonamides. Both forms of therapy have given good results but those with penicillin have been more spectacular. In treating gonorrhea complicating pregnancy a total dose of 100,000 to 150,000 Oxford units of penicillin is given in about thirty hours. In treating chronic gonorrhea in pregnancy penicillin may also be employed, the procedure and dose being the same as in acute gonorrhea. When sulfathiazole is used the author supplements it by local vaginal treatment and a Lugol's solution douche given at home. The local vaginal treatment consists in the application of an aqueous metaphen solution 1-1,000 applied to the cervix and vagina; for home use a Lugol's solution douche is prescribed. The patient is instructed to use one teaspoonful of the Lugol's solution in two quarts of boiled water. The

prior to operation. It was difficult to differentiate the cases from those of premature separation of the placenta. 20 references.

## A SEVEN-YEAR REVIEW OF ECLAMPSIA WITH SPECIAL REFERENCE TO TREATMENT WITH VERATRUM VIRIDE

LT. (J.G.) GEORGE G. GREENE (MC) USNR.

Am. J. Obst. & Gynec., 50: 427-30, October, 1945

The author believes that veratrum viride should still have a definite place in the therapy of eclampsia. In substantiation of this statement he refers to the Department of Obstetrics at the University of Cincinnati, where 120 cases treated by veratrum viride showed a maternal mortality of only 1.6 per cent. The author used this drug during the years 1941-42 in fourteen cases and all the patients recovered. It was found that treatment resulted in an immediate cessation of convulsions in 50 per cent or more of the cases, and in a short time the patient became rational and responded to questions. By way of comparison the author cites a maternal mortality of 26 per cent in 150 cases of eclampsia treated by various other methods in the same hospital between 1936 and 1942.

Veratrum viride acts as a cardio-inhibitor, vasodilator and antipyretic. It is toxic in large doses and must be given carefully. Toxic reactions include sudden drop in blood pressure and pulse rate, nausea and vomiting, and coma. These may be counteracted by gastric lavage or atropine. Under these conditions it is best to discontinue the treatment and resort to some other measure. The preparation used in this study was Veratrone, in doses of 3 to 10 minims, given hypodermatically.

Of the 150 cases reviewed, 129 were Negro and 21 white, a ratio of nearly 6 to 1. Many of these never attended a prenatal clinic. Over 50 per cent were women 20 years of age or younger. It would seem that true eclampsia is more frequent in this age group and is due to lack of care. Of the 150 cases 104 were primigravidas. The older patients, who had had several children and were in the later years of childbearing, were found to have had chronic kidney damage for some time. In this group it is found that veratrum viride is not of much value. In over half of the patients onset of eclampsia was in the antepartum period.

During the seven years studied every method of treatment known seemed to have been given. Many sedatives were used and in the earlier years many supportive measures were employed. Digitalis was used in five of the years reviewed and is still being given in some hospitals. The author is of the opinion that it has no place in the treatment of eclampsia unless decompensation or auricular fibrillation is present. In 1937 many cesarean sections were performed, and it was then that the mortality reached its highest peak. Nine sections were done out of 20 cases that year; 7 of the 9 expired. This emphasizes the need for control of eclampsia before any operative measure is attempted.

Delivery should not be attempted until convulsions are controlled and the patient rational for one or two days. Many patients go into labor spontaneously during that period. If not, medical induction or rupturing of the membranes can be carried out. If the patient is a primipara near term, with a closed, thick cervix, a cesarean section can be considered and performed rather safely, provided the eclamptic state has been controlled for a time.

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douche is used at a temperature of 110° at a low pressure and a nozzle is not used. The author has treated in this manner 228 cases of gonorrhea complicating pregnancy without a single case of ophthalmia neonatorum.

Among 1250 consecutive admissions to the maternity ward of the Jefferson Hospital 132 patients or 10.6% had trichomonas vaginalis infestation; 67 or 5.4% had gonorrheal infection, while 24 or 1.9% had both trichomonas vaginalis infestation and gonorrheal infection.

In discussing the treatment of trichomonas vaginalis infestation it is suggested that care be exercised when using an insufflator and antiseptic powder since several cases of embolism have been reported following this procedure. The powder should not be blown into the vagina under too much pressure.

For the treatment of vaginal moniliasis the application of two per cent aqueous Gentian violet to the vaginal mucosa is recommended.

Syphilis, chancroids, lymphogranuloma venereum, granuloma inguinale, and tuberculosis are also discussed.

## SICKLE-CELL ANEMIA COMPLICATED BY PREGNANCY

MARY SPIVACK

Am. J. Obst. & Gynec., 50: 442-46, October, 1945

Published cases of sickle-cell anemia complicated by pregnancy are, according to the author, scarce. She gives the case history of one which she had the opportunity to study long before term. From the literature it is observed that in several cases the nature of the anemia, or the disease itself, was not diagnosed until after the patient's admission to the hospital either because of the onset of labor or of an intercurrent infectious disease. In few instances correct diagnosis was not made until postmortem was carried out.

Sickle-cell anemia is a familial and hereditary disease. Diagnosis should not be difficult if the salient features of the disease are kept in mind—attacks of muscular and joint pains, weakness and elevation of temperature in the presence of anemia. The Negro race is especially susceptible to the ailment. The association of the disease with pregnancy is not frequent; only 17 cases have been described so far. According to several observers, pregnancy is unfavorable to the anemia and the mortality is high; about 33 per cent of the reported pregnant patients died during pregnancy, labor or the puerperium. No specific treatment is known to exist, though blood transfusions improve the patient's condition, temporarily at least.

The average age of patients with this blood dyscrasia is 22.4 years, the oldest recorded being 30 years of age. The author believes that the 35 year old patient in her reported history is the only one to reach that age and the duration of the anemia the longest thus far described. It appears from this study that gestation does aggravate the condition, as only in the beginning of the patient's pregnancy

did the red blood count reach its low ebb of 1,500,000 per cubic millimeter. Unlike the majority of patients with the disease, this one did not run a febrile puerperal course, in spite of long labor and an operative delivery (midforceps and episiotomy). This, the author thinks, was possibly due to the fact that the woman was well prepared for her ordeal by blood transfusions, given prophylactically as part of the prenatal care, and at the onset of labor. Six months after childbirth this patient was in fair health. At the age of three weeks, the child had a red count of 5,310,000 and a sickle-cell trait.

Blood transfusions, while they do not cure the patient nor alter the prognosis, are of paramount importance in bringing these cases through the dangerous period of pregnancy and labor. Only further progress in the knowledge of this dyscrasia and its causes may render treatment more specific and the prognosis more favorable.

One figure. Five references.

## A CASE OF ARRHENOBLASTOMA COMPLICATING PREGNANCY

C. PHILIP BRENTNALL

J. Obst. & Gynaec. Brit. Emp., 52: 235-40, June, 1945

The case described in this report appears to be unique, for although some 60 cases of this type of tumor have been recorded, not one has occurred associated with pregnancy.

The patient, Mrs. F., 26 years of age, came to the outpatient department of the Saint Mary's Hospitals in July, 1943. She had a masculine distribution of hair, a masculine voice and figure, except that the abdomen was distended by a 7 months pregnant uterus and the breasts were enlarged and showed all the usual signs of pregnancy. The clitoris was much enlarged but there was no alteration in the labia. Vaginal examination revealed the presence of a smooth-surfaced tumor, about the size of a Jaffa orange, separate from the uterus, situated in the pelvis and pushing the cervix forward into close relation with the pubes.

Her previous medical history was without particular interest. During the previous April, the manifestations of masculinization began to appear with growth of hair on the abdomen, chest, face, arms and legs. Acne and boils developed on her face and shoulders. Her voice deepened. It was impossible to discover any psychological alteration.

From the previous February until 3 weeks after delivery she had glycosuria. She appeared to be an example of the "Achard-Tiers syndrome," sometimes referred to as "the diabetes of bearded women." She was also very anemic.

At delivery, a cesarean section was performed and the tumor, a new growth of the right ovary, was removed. Lactation was established satisfactorily and uterine involution and lochial discharge were about normal for a cesarean

section case. Three months after delivery there was no change in her voice, yet the masculine distribution of hair was gone except for a suggestion of a mustache.

There is no doubt that this is a typical case of arrhenoblastoma with characteristic symptoms and signs except where these were interfered with by the pregnancy. The tumor, upon examination, was found to fall in the histological group of ovarian tumors consisting largely of cellular fibromatous tissue which is sometimes so cellular as to be described as sarcomatous.

The child appeared normal except for the external genital organs. The clitoris was much enlarged and the glans, prepuce and frenulum well-formed. The labia majora were enlarged and corrugated; the labia minora as such were absent. The urethra opened at the base of the clitoris and behind this the perineum extended unbroken to the anus. A discharge of blood from the urethra on the 4th day of life was strong presumptive evidence of the existence of a uterus and a vagina opening into the urethra, the child therefore being a female pseudohermaphrodite.

The author studies the question of how this variety of female pseudohermaphrodite develops. It is suggested that the androgen from the ovarian tumor did not reach the fetus in effective quantity until the 3rd month of fetal life. By this time the female hormone of the fetal gonad had already produced some reactions in the accessory sex organs.

Complete knowledge of the child cannot be had for several years. 6 references. 1 plate. 9 figures.

## CARCINOMA OF THE CERVIX COMPLICATED BY PREGNANCY

J. ROBERT WILSON

*Am. J. Obst. & Gynec.*, 50: 276-83, September, 1945

Carcinoma of the cervix is rare in pregnancy and the lesion may not be discovered until it has progressed too far to hope for cure. According to a series of reports in 1937, the incidence of this condition complicating pregnancy is only about one case in three thousand. This is not surprising as carcinoma of the cervix in the nonpregnant is low in the younger age groups into which the majority of childbearing women fall.

At the Chicago Lying-In Hospital only six patients have been treated for carcinoma of the cervix in pregnancy since 1931. A total of 39,719 patients were delivered in this period; therefore the incidence of the disease in that institution was one in each 6,620 deliveries, or 0.015 per cent. All lesions were of squamous-cell origin except one, which was adenocarcinoma. Of these only three were eligible for consideration. Two (67 per cent) survived longer than 5 years after treatment, but only one is free from evidence of carcinoma.

Bleeding during early pregnancy persisting for more than one week, despite rest, may be due to a malignancy. Examination in such a case is a necessity. The signs during pregnancy are the same as those characteristic of a similar lesion in the nonpregnant uterus and biopsy of any suspicious area or lesion of the cervix should be done. An accurate pathologic diagnosis on tissue removed is of the utmost importance. Benign lesions should not be treated during pregnancy and in the case of questionable diagnosis, the patient should not be subjected to intense irradiation therapy.

The prognosis for carcinoma of the cervix discovered during pregnancy and properly treated, appears to be as good as in the nonpregnant individual. There is a high survival rate, as usually diagnosis should be made early in the course of the disease. Fetal prognosis is dependent primarily upon the stage of pregnancy at the time the carcinoma is discovered.

Because of the small number of cases observed, no definite conclusion has been reached by the author as to the most effective treatment for these cases. However, it is conceded that cervical cancer is best treated by a combination of radium and deep X-ray therapy. The amount of irradiation necessary to destroy the lesion is comparable to that in the absence of pregnancy, but pregnancy may require alteration in the routine of administration. Postirradiation pelvic lymphadenectomy may improve the results. If the lesion is extensive, involving a large part of the cervix, dilatation will not occur, but its friability may result in hemorrhage at delivery. For this reason abdominal delivery is indicated. However, the danger of infection is increased in these cases, since a sloughing cervical lesion is always infected. Under these circumstances cesarean subtotal hysterectomy is advised. Administration of sulfonamides by mouth reduce danger from infection.

Fetal prognosis depends primarily upon the stage of the pregnancy at the time the carcinoma is discovered. Initiation of therapy before the period of viability must sacrifice the infant. If the lesion is found at a later period, the plan of treatment may be designed to save the baby, unless the method would decrease the chance of destroying the neoplasm.

The author gives a summary of treatment to be carried out during the three trimesters of pregnancy. Twelve references. Two tables.

## CONGENITAL ABSENCE OF THE SACRUM AND COCCYX COMPLICATING PREGNANCY

CAPTAIN WILLIAM BERMAN, M. C. U. S. A.

Am. J. Obst. & Gyn., 50: 447-50, October, 1945

This is the case history of a patient with a rare congenital pelvic abnormality—total absence of the sacrum and coccyx. There were also urologic complications,

manifested by incontinence, due to lack of sphincter control. In recent years the more common usage of roentgen pelvimetry has made possible the discovery of unsuspected pelvic abnormalities, thus aiding in the management of the cases during labor.

The case presented in this article was that of a twenty year old primipara, first seen in the prenatal clinic when sixteen weeks pregnant. The patient was aware of the skeletal anomaly. She gave a history of being incontinent and partially involuntary, although there was some tone to the rectal sphincter muscles. The vertebral column was straight, but terminated at the junction of the last lumbar vertebra and the pelvic girdle. There was moderate atrophy of the thigh muscles, and this condition was quite marked in the muscles of leg and foot. X-ray showed the fetal head above the pelvic inlet, and it appeared full term in size. The inlet was asymmetrical and did not correspond to any of the pure types of pelvis. It appeared cylindrical, with the greatest diameter of the cylinder running anteroposteriorly. The head seemed too large for the inlet. A diagnosis of relative cephalopelvic disproportion was made and it was deemed best to give the patient a test of labor. This was done, but in about thirty-six hours she had made no progress.

Under spinal anesthesia, a low classical cesarean section was done, and a living infant delivered. The child, however, expired shortly after birth. Autopsy revealed that the baby had a congenital heart lesion and complete atelectasis of the lungs. X-ray of the spine showed no bony abnormality. The patient had an uneventful postoperative course.

A few months later, she was operated upon for her incontinence. A cystocele repair was done and two portions of the sheath of the rectus abdominis muscles were brought under the bladder for support, according to the method of Aldridge. No great improvement was derived from this procedure.

At the time of the report, the patient was again pregnant, and there had been no change in her prepregnant status. It is problematical what effect the second pregnancy will have upon the plastic repair done previously.

Three figures. Two references.

## PATHOLOGY OF LABOR AND PUERPERIUM

### STRANGULATED HERNIA CONTAINING PREGNANT UTERUS AT TERM

CHARLES E. BOYS

Am. J. Obst. & Gyn., 50: 450-52, October, 1945

Cases of strangulated hernia containing a pregnant uterus at or near term are rare. In medical literature only five case reports were found by the author. When this condition does occur it is a real obstetric problem particularly when most or all of the pregnant uterus is strangulated in a hernial sac. In the earlier months the pregnancy is often terminated by spontaneous or therapeutic abortion.

Because of the apparent rarity of the condition, the author reports his case. The patient was a 37 year old woman, para eleven, at term. She had been in unusually severe labor for fourteen hours, without measurable progress, when first seen by the writer. She had had a supraumbilical hernia for several years, which had caused difficulty in three previous labors, especially the last. On examination a tumor protruded from the upper abdomen, through a median cleft in the abdominal wall, above the umbilicus. Between pains the mass extended 17 cm. above the normal curve of the abdomen, and during pains it was 7 cm. higher. Enormous varicosities were present in both lower extremities, but there were no palpable thromboses. X-ray examination disclosed a full term fetus, with the head not engaged. Uterine contractions recurred at from three to five minute intervals and were unusually violent, due partly to the strangulation. Rectal examination failed to reveal any fetal presenting part, and no effacement or dilatation of the cervix, which was very high. No vaginal bleeding evident. Mechanical attempts to reduce the hernia were futile.

A classical cesarean section was carried out at once. The tumor was well exposed and found to consist of the entire fundus and about half of the corpus of the uterus, with enormously varicose broad ligaments. Reduction of the mass was impossible without enlarging the fascial ring. On incising the corpus, a large placenta was found immediately underneath. The buttocks and lower extremities of the fetus were incarcerated under the placenta, which was removed first. The infant weighed ten pounds fourteen ounces and was in good condition. The surplus tissue of the hernial sac was excised, the peritoneum sutured and the fascia closed by imbrication. By the tenth postoperative day there was some breaking down of the superficial part of the wound and the hernioplasty was only partially successful. However, in 18 months the patient gave birth to her twelfth child, following a three hour labor, without incident.

One figure. Five references.

manifested by incontinence, due to lack of sphincter control. In recent years the more common usage of roentgen pelvimetry has made possible the discovery of unsuspected pelvic abnormalities, thus aiding in the management of the cases during labor.

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Three figures. Two references.

GAS BACILLUS INFECTION OF THE UTERUS TREATED WITH  
PENICILLIN

GWEN S. HUDSON AND M. PIERCE RUCKER

Am. J. Obst. &amp; Gyn., 50: 452-55, October, 1945

Penicillin is theoretically the drug for the treatment of *Clostridium welchii*, according to these authors, because it is effective not only against this bacillus, but also against many of the organisms that are frequently associated with it in postabortal infections. In wound infections, penicillin has been found to be effective against gas bacilli in the blood stream, but has no effect upon the bacilli growing in dead tissue. Débridement is as necessary when penicillin is used as it was formerly. Treatment of postabortal and postpartum infections with penicillin should be combined with local treatment.

The article goes on to describe the nature of the gas bacillus, and states that in the 45 years combined experience of the authors, they have seen only three proven cases and one suspicious case of *Clostridium welchii* infection. The Welch bacillus is more frequent with abortions than with full term deliveries and criminal abortions furnish ideal conditions for that type of infection, for obvious reasons.

The diagnosis depends upon demonstrating the organisms either in blood cultures or in cultures from the uterus. It should be suspected in any severe and rapidly progressive infection, especially if there is evidence of gas formation. This suspicion is heightened when an abortion has been induced outside of a hospital.

The course of the disease is so rapid that no time should be lost in beginning treatment. The patient may die within sixteen hours from the time of interference.

A case report is given of a patient with *Clostridium welchii*, in which treatment with penicillin apparently confined the infection to the uterus. However, it had no effect upon the process within that organ. The uterus continued to enlarge and was exquisitely tender until the patient was given, in addition, sulfadiazine and local treatment with zinc peroxide. Recovery was then uneventful, except for an attack of hepatitis on the 17th postabortal day, possibly incident to the sulfonamide therapy. She was discharged well twenty-nine days after the abortion.

Eight references.

## CHANGES IN NUMBERS OF CIRCULATING BLOOD PLATELETS FOLLOWING EXPERIMENTAL TRAUMATA

HELEN PAYLING WRIGHT

J. Obst. & Gynaec. Brit. Emp., 52: 253-58, June, 1945

At present, very little is known of the factors which bring about an increase in the numbers of circulating platelets in the postoperative period, often resulting in thrombosis. The author presents, in this report, a study of these factors based upon experimental work with rabbits. The component parts of major operations were subdivided into stages in order that the effects of various constituent procedures might be studied separately.

Six full-grown rabbits were used for these operations with a period of no less than 5 weeks between operations. Observations were made upon the number of platelets and red cells before each operation, immediately after (within an hour), and on the 4th, 7th, 10th, 14th and 21st postoperative days. Blood for these counts was obtained by razor cuts in the marginal ear veins of the rabbits.

The graded operations performed were as follows: bleeding with minimal surgical trauma, simple skin incision, skin and muscle incision, non-surgical destruction of muscle tissue by the injection of 2 c.cm. of a 2.0 per cent suspension of Neosyl (aluminum silicate) in normal saline into the thigh muscles, celiotomy with manipulation of the gut, celiotomy with autolysis of muscle strip, non-surgical sterile irritation of the peritoneum, and splenectomy.

Results showed that in all stages the red-cell counts remained steady throughout. The platelets, however, in all instances showed an increase in numbers, reaching a maximum in 7 to 10 days and thereafter returning to normal by the 21st day. The extent of the rise appeared to bear a direct relation to the severity of the operation.

The author discusses the observations of other workers on this subject and from their findings and her own, draws the following conclusion:

"It would seem, therefore, that these graded animal experiments support the hypothesis that tissue damage resulting in autolysis is an important factor in initiating the increase in platelet numbers in the postoperative period, and that additional light may well be thrown upon the nature of the ultimate stimulus by the further investigation of tissue extracts and their chemical components."

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The diagnosis depends upon demonstrating the organisms either in blood cultures or in cultures from the uterus. It should be suspected in any severe and rapidly progressive infection, especially if there is evidence of gas formation. This suspicion is heightened when an abortion has been induced outside of a hospital.

The course of the disease is so rapid that no time should be lost in beginning treatment. The patient may die within sixteen hours from the time of interference.

A case report is given of a patient with *Clostridium welchii*, in which treatment with penicillin apparently confined the infection to the uterus. However, it had no effect upon the process within that organ. The uterus continued to enlarge and was exquisitely tender until the patient was given, in addition, sulfadiazine and local treatment with zinc peroxide. Recovery was then uneventful, except for an attack of hepatitis on the 17th postabortal day, possibly incident to the sulfonamide therapy. She was discharged well twenty-nine days after the abortion.

Eight references.

## MATERNAL DEATHS DUE TO INFECTION

MINNESOTA MATERNAL MORTALITY COMMITTEE

Minn. Med., 28: 635-40, 1945

A study of all maternal deaths in Minnesota from July 1, 1941, through June 30, 1942, showed that 26 deaths were due to infection. The ratio of primigravidae to multigravidae was 8 to 18. The Committee felt that 18 of these 26 deaths were preventable, seven not preventable. In the remaining case it was impossible to determine the preventability. It was concluded that practically all of the preventable deaths were the responsibility of the attending physician. The causes of death were as follows: abortion, 11 deaths, of which five were due to peritonitis, three to septicemia and one each to tetanus, pyemia and septicemia (extragenital infection); seven of the full or near full-term deaths were due to pulmonary embolism, three each to peritonitis and puerperal sepsis, and one each to mesenteric thrombosis, septicemia with pneumonia, and septicemia (extragenital infection). Details of the 26 deaths are given. They reveal a definite lack of proper prenatal care in several instances. Deaths following desperate operative delivery in three instances could have been avoided by examination for cephalo-pelvic disproportion before the onset of labor. In two instances death could have been averted by elective cesarean section had the previous obstetrical histories of these women been taken. Lack of preparation of the patient for surgical procedure, lack of blood determination and indiscriminate use of general anesthesia at delivery were noted in several cases. Only 3.5 per cent of the patients who died had received adequate postpartum care. The chemotherapeutic attack in most of the cases was not fully utilized either in respect to time of administration, dosage or choice of drug.

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## PATHOGENESIS OF POSTABORTAL PERITONITIS. A STUDY OF 61 CASES

HENRY C. FALK AND GEORGE BLINICK

Am. J. Obst. &amp; Gynec., 50: 168-174, 1945

This study is devoted to an analysis of the pathogenesis and associated pathological findings in 61 cases of infected abortions in which the infection spread from the uterus to the peritoneum and produced a general peritonitis. Patients with parametritis and an associated peritoneal or local pelvic peritonitis and those with peritonitis secondary to perforation of the uterus are not included in this series. Examination at autopsy revealed that the most common pathway of infection from the endometrium to the peritoneum was by direct extension

through the tubes. This mode of infection spread was found in 66 per cent of the cases. Infection spread by way of the parametrium in 10 per cent, the myometrium in 7 per cent, and in other combinations in 17 per cent of the cases. The last mentioned group included; (1) six patients with endometritis, salpingitis, parametritis and peritonitis in which the pathway of infection was not clear; and (2) four patients, with endometritis, abscess of the myometrium, salpingitis and peritonitis, who, although the tubes were probably the chief pathways of extension, were not included in this group because of the questionable etiology of the peritonitis. Ovarian abscess (type unrecorded) was found 17 times. Thrombophlebitis of the uterine or ovarian veins, or both, occurred in 20 patients. It was present more often in patients with parametritis or myometritis alone or in combination than in those with salpingitis alone. In five patients embolic abscesses of the lungs were observed. No other sites of embolization were found. Several case reports illustrative of each route of infection are presented.

## THE NEWBORN

### SHOULD WE CHANGE OUR PRESENT STANDARD ON INFANT VIABILITY?

R. L. HAAS

Am. J. Obst. & Gynec., 50: 406-11, October, 1945

This article begins with the question as to what constitutes the lower limit of viability of the premature infant. The literature on the subject has been carefully reviewed by the author and three cases of very premature babies from his hospital are recorded.

On the basis of duration of pregnancy, a fetus which has remained in utero twenty-six to twenty-eight weeks is generally said to be viable. A table of the period of gestation at which the reporting of stillbirths is required in different States of this country is given. The standard set by law varies among the States, but usually birth and death certificates are required for infants when the duration of gestation is five months or more; this is in accord with the Model Vital Statistics Act of 1941. Every effort should be made to save even those babies which appear nonviable by these standards.

The prognosis for survival of an infant varies with its weight. Those weighing less than 1,000 grams (2 pounds 3 ounces) do not have a good outlook, but a survey of the literature shows fifty-four surviving cases on record. The smallest surviving infant weighed 420 grams. In 1940, two babies weighing less than 1,000 grams were born in the University of Michigan Hospital. The pregnancies were interrupted artificially at six or six and a half months and deliveries were spontaneous. One infant weighed 705 grams and the other 934 grams, when weighed on the ninth and sixteenth days respectively. Both were kept in incubators with continuous oxygen for nearly two months. Inhalations of 5 per cent carbon dioxide were frequently used the first few weeks. There was a third infant born in 1944, weighing 830 grams sixteen days after birth. This child was born during the sixth month, the membranes rupturing spontaneously and labor ensuing two weeks later. The care of the three infants was the same. Particular attention was given in suctioning off aspirated mucus and amniotic fluid. Five per cent glucose water in  $\frac{1}{4}$  ounce quantities given every two hours until well taken. Then a formula was substituted, feedings being carefully administered. Vitamins A, C and D, and iron, were begun as soon as the feedings were established.

The follow-up in the first two cases showed that the first child, who was the smaller, made good progress and at three years was healthy and active. The second case did not do as well, having some feeding difficulties at six months; had thrush and some trouble with eyes. However, at 23 months the baby weighed 25 pounds and seemed healthy. The third infant weighed about 6 pounds when about 3 months of age.

The problem of whether the prospects for satisfactory mental and physical development of very small premature infants justifies the care they require has received considerable attention and it shows that, excluding cases of birth injury, their development is comparable to that of normal children. Physical growth may lag somewhat. When hospitals can be better equipped for the care of these babies, their care will become less formidable. Caudal anesthesia, which minimizes trauma to the fetal head, and proper transfusions will result in a rise in the number of prematures born alive.

One thousand grams (2 pounds, 3 ounces) is proposed as the lower limit of viability for statistical purposes. The number of recorded infants weighing less than this amount who have survived is not great; yet they are enough to show that every infant, no matter how premature, deserves the opportunity for life. 2 tables. 15 references.

## AETIOLOGY OF HAEMOLYTIC DISEASE OF THE NEW-BORN

R. J. WALSH

Med. J. Australia, 2: 33-9, 1945

Serological investigations were made of 106 families selected because of the occurrence in them of hemolytic disease of the new-born, stillbirths of unexplained etiology, repeated miscarriages, or physiological jaundice. The diagnosis of hemolytic disease of the new-born was made only if one of the following criteria was established: (a) severe jaundice at or shortly after birth, increasing in degree and associated with a reduction of the erythrocyte count and hemoglobin figure below normal, or with the presence of erythroblasts and other immature erythrocytes in the peripheral blood stream; (b) severe anemia without jaundice appearing at or shortly after birth; (c) post-delivery evidence of hydrops fetalis, either macroscopic or histological. In 90 families ABO and Rh typings were performed on the father, mother, some of the living children and, in most cases, on the affected child. In the other 16 families these typings were made on the mother and affected child. In 83 (92 per cent) of the 90 families the mother was found to have Rh-negative blood and the father Rh-positive blood. In the 16 families in which only the mother and affected child were examined, the mother had Rh-negative blood in 14 and Rh-positive blood in two instances. An Rh agglutinin was found in the serum of 48 per cent of the 106 mothers. The severity of the disease in the child was not related to the presence of the Rh agglutinin in the mother. In general, the frequency of occurrence and the severity of the disease increased with an increasing number of pregnancies, but some exceptions were noted. Only four of the 26 women whose pregnancy terminated in stillbirth of unexplained etiology had Rh-negative blood (the husbands of all four had Rh-positive blood), but the bloods of nine of the 23 women with a history of repeated miscarriages of unexplained etiology were Rh-neg-

ative. Only one of the twelve mothers whose children developed physiological jaundice was found to have Rh-negative blood, and in no instance was an irregular agglutinin detected in the mother's serum. The mechanism by which the Rh factor passes across the placenta and immunizes the mother is discussed. No agglutinin was demonstrated in the blood of eight infants who were examined, but intravascular agglutination was noted in several of these cases. The possibility is advanced that the colostrum plays a part in causing destruction of the infant's erythrocytes or that extracorporeal Rh substance may absorb some Rh agglutinin before it reaches the Rh-positive erythrocytes.

## Rh INCOMPATIBILITY AS A CAUSE OF MENTAL DEFICIENCY

### EDITORIAL

Brit. Med. Jour., 188-189, August 11, 1945

In this editorial recent evidence is reviewed pointing to the fact that a substantial amount of mental deficiency is the result of Rh incompatibility. In the first place, reference is made to the work of Yannet and Lieberman showing that in 56 undifferentiated idiots (that is idiots in whom none of the known causes of idiocy was demonstrable) there were no fewer than 11 who were Rh positive with Rh negative mothers. If we were to draw a random sample of 56 mothers and children from the general population, the expected number, accepting the proportion of Rh-negative persons as 15%, would be 5.15—less than half the number observed. In another comparable study by Snyder, Schonfeld and Offerman, in 11 out of 68 similar undifferentiated defectives the Rh reaction of the mother was negative and the offspring positive. Adding the two series together the number is 22 out of 124. The expected number in a random sample of 124 is 11.40. The odds against so big a difference as this arising with the accidents of sampling are nearly 600 to 1. The editorial concludes that the evidence in favor of the hypothesis is thus very strong, but the figures are not sufficient yet to allow any close estimates to be made as to how much mental deficiency is due to this cause. Should further work reveal a figure similar to that indicated in these first series, then Rh incompatibility would be about half as important numerically as mongolism as a cause of mental deficiency among institutional defectives.

## THE Rh FACTOR IN OBSTETRICS

JACOB HALPERIN, MENDEL JACOBI AND ALVIN DUBIN

Am. J. Obst. &amp; Gynec., 50: 326-30, September, 1945

The authors urge the adoption, by obstetric institutions, of the routine determination of the Rh factor in all pregnant women. From a study of 3,885 deliveries, they found that discrepancy in the Rh factor is the most potent cause of intragroup transfusion reactions in Rh-negative women, particularly if they have recently been pregnant. Also, in accord with the literature, they found that, with few exceptions, fetal erythroblastosis results from a mating of an Rh-negative female with an Rh-positive male.

In the first 500 consecutive patients in whom the Rh factor was determined, there was an incidence of 13.2 per cent of Rh-negative women. An incidence of 65.7 per cent of these so far delivered showed some form of erythroblastosis symptoms. In these erythroblastotic newborn infants, males predominated.

New statistics and analyses are presented in this report which show that the male fetus is more susceptible to erythroblastosis fetalis than the female in the proportion of approximately 3:1, and in fatal cases approximately 5:1. The chances for a female to recover are, therefore, so much greater. This discovery offers one means of prognosticating the outcome. The explanation for the greater severity of the disease in males is difficult to explain on a sex-linkage basis. There may be another genetic factor involved which is not yet known. 11 references.

(The high incidence of "erythroblastosis symptoms," 65.7 per cent, in the offspring of Rh negative mothers, as reported in this article, will provoke surprise in most readers. A partial explanation is afforded, perhaps, by the fact that the authors include what is usually termed "physiologic jaundice" among such symptoms. Even then, this finding is difficult to understand and is at great variance with the usual experience that only one in forty or so of the offspring of Rh negative mothers (with Rh positive fathers) manifest erythroblastosis.

The authors' demonstration that the male fetus is more vulnerable to erythroblastosis than the female is in keeping with the curious preferential death rate which is active in utero against the male. Crew (Trans. Edinb. Obst. Soc., 47, 122, 1927) estimates that the ratio of males to females at the onset of pregnancy is 170:100. In a study of 1200 specimens of abortion in the Carnegie Institute of Embryology, Schultz (Contrib. to Embryol. No. 56, pp. 177-191) found a ratio of 110:100. Since it is well known that this ratio at term is 105:100, the conclusion is inescapable that abortion strikes the male fetus more frequently than the female. And in general about 60 per cent of abortions and the same percentage of stillbirths are of the male sex. That erythroblastosis should show a similar preferential death rate is of much interest.

The authors' contention that Rh determinations be done on all pregnant women is, of course, a gospel that needs preaching far and wide. There is also need for an educational program among all physicians in respect to the necessity of performing such typing on any person of any age prior to blood transfusion, particularly females. The occasional tragedy which will inevitably result from neglect of this dictum was exemplified by a patient who was recently delivered in my clinic. Routine typing showed her Rh negative and her hus-

band Rh positive, but since she was a primigravida and since erythroblastosis is uncommon in primigravidae, a normal baby was anticipated. The baby at birth, however, showed a combination of the hydrops and icterus types of the disease and died soon after delivery. Further history taking revealed the fact that several years previous she had had a blood transfusion at another hospital for intractable nose-bleed. The chances are six out of seven that the donor was Rh positive. Had her Rh negativeness been established before the transfusion and had Rh negative blood been used the present tragedy would probably have been averted. This case teaches another important lesson: when an expectant mother is reported as Rh negative, always ask if she has ever had a blood transfusion.—Ed.)

## CONGENITAL DEAFNESS AND CATARACT FOLLOWING RUBELLA IN THE MOTHER

FRANZ ALTMANN AND ALBERT DINGMANN

Arch. Otolaryngol., 42: 51-2, 1945

Following a brief review of the literature a case report is presented. The subject's mother had contracted German measles during the latter part of the second month of pregnancy. When the child was four months old, a congenital cataract was removed from his right eye. At the age of ten months he still showed no recognizable reaction to sounds. The vestibular function was normal. No malformations or defects other than the unilateral cataract and complete loss of cochlear function were found. This is the first time, according to the authors, that the combination of deaf-mutism and cataract has been reported in the literature. It had been thought that the nature of the defect in the child depended upon the stage in pregnancy in which the mother contracted rubella. As it had been found that the average time during pregnancy was 2.3 months in the case of the children showing deaf-mutism and 1.4 months in that of children with congenital cataract, the present case shows that time of the onset of rubella cannot be the only determining factor.

## SO-CALLED GERMAN MEASLES DEAF-MUTISM, WITH PATENT DUCTUS ARTERIOSUS

D. G. R. VICKERY

Med. J. Australia, 2: 57, 1945

This case report deals with a child whose mother had had German measles in the third month of pregnancy. At the age of four years he weighed 27 pounds and exhibited cardiac dwarfism, congenital cardiac disease and deaf-mutism.

He did not respond to the spoken voice but could hear handclaps, whistles and other sharp noises.

### - SO-CALLED GERMAN MEASLES CATARACT, WITH CONGENITAL CARDIAC DEFECT

D. G. R. VICKERY

Med. J. Australia, 2: 57, 1945

The patient was four years old at the time of this report. Her mother had suffered from German measles in the second month of pregnancy. The child's birth weight had been 6.5 pounds and her present weight was 23.75 pounds. A cataract of the right eye had been aspirated when she was a year old. She had cardiac dwarfism. Cardiac findings suggested a patent interventricular septal lesion and possibly a patent ductus arteriosus. Intelligence was normal.

### A CASE OF THIRD-GENERATION SYPHILIS

C. J. V. HELLIWELL\*

Brit. Med. Jour., 186, August 11, 1945

The case history of a 14 year old boy with congenital taboparesis is presented with convincing evidence to show that it represents a case of third-generation syphilis. The boy had a typically tabetic gait due to spasticity of the lower limbs. The right pupil was dilated and did not react to light, while the left was normal and reacted to light. The blood Wassermann reaction was positive. The cerebrospinal fluid findings were as follows: Wassermann reaction+++; Lange, 5553210000; cells, 20 per c.mm.; total protein, 30 mg. per 100 c.cm.; globulin, increased. The boy was grossly defective mentally.

On investigating the rest of the family—the two other children, the father, and the mother—the only one who showed a positive Wassermann reaction was the mother. She avowed that she had never had syphilis, nor any treatment; but that both her parents had died as a result of the disease. This would indicate that she herself was a congenital syphilitic, even though she shows no signs, apart from that complacent facies which is so often seen. The father had been a blood donor for more than twenty five years; it is therefore reasonable to assume that his blood Wassermann reaction had been negative all that time and certainly during the twenty years that he had known the mother. Both the daughter, aged 17, and the younger son, aged 12, showed no signs of the disease

and were brilliant scholars. It can thus be stated that these three members of the family were, and always had been, free from syphilis; and should the mother have acquired it at all it would have been manifested in one or all of them. The evidence therefore shows that the mother is a congenital syphilitic who has given birth to a third-generation congenital syphilitic.

## THE EFFECT OF RESPIRATORY STIMULANTS IN THE NEWBORN INFANT

KHA TI LIM AND FRANKLIN F. SNYDER

Am. J. Obst. & Gynec., 50: 146-153, 1945

The purpose of this investigation was to determine the effect upon the *normal* newborn infant of various respiratory stimulants, including alpha-lobeline, coramine, metrazol, caffeine, and cyanide. In these experiments on rabbits it was aimed to take into account the peculiarities of the newly born animal in response to these agents and to eliminate complicating factors commonly associated with clinical trial. The observations are confined to 83 newborn rabbits obtained from 41 litters. In one group of 57, pentobarbital sodium was injected subcutaneously one hour before the respiratory stimulants were tested. In the others, premedication was omitted. An additional series of 21 rabbits was studied during the later neonatal period at a time when respiratory responses were well established. Various amounts of the drugs were injected into the external jugular vein. For control injections Ringer's solution was used. It was difficult to demonstrate significant stimulation of respiration following the administration of alpha-lobeline, coramine, and caffeine; following metrazol or cyanide, the slight stimulation was transient, lasting less than a minute. The range between the effective dosage and that which caused convulsions was very narrow. This hazard was particularly noticeable in the presence of pentobarbital premedication. In several of these instances the effective dose resulted in convulsions. No marked change was noted in the range of safe dosage in the series of sucklings. Injury resulting in death frequently followed convulsions which occurred after administration of alpha-lobeline, coramine or caffeine. After metrazol or cyanide the animals survived despite the occurrence of convulsions.

## THE BIRTH OF A TWENTY-POUND INFANT

J. J. GWIN

J. Tenn. State Med. Assoc., 38: 266, 1945.

The mother of the subject of this case report was a white woman with a history of three previous pregnancies resulting in three healthy babies. The first weighed nine pounds at birth, the second 9.5 pounds, and the third 12 pounds. The mother was very obese (height, five feet, four inches; weight, 245 pounds) and had disregarded dietary instructions given at various times during her fourth pregnancy. Nine days after the expected date of confinement, daily doses of thyroid extract and magnesium sulphate were given. Three days later labor was induced by doses of obstetrical pituitrin. Ether analgesia and assists were used at delivery. The head and trunk were extricated with only moderate difficulty, but the shoulders and pelvic girdle were extricated with extreme difficulty. The cord (ca. 29 inches long) was wrapped once around the neck. The baby was dead at birth. No fractures were found. The infant weighed twenty pounds and the afterbirth 4.5 pounds. The mother sustained only a slight mucous membrane laceration and had an uneventful convalescence.

## OPERATIVE OBSTETRICS

### DYSTOCIA DUE TO THE SHOULDERS

CHARLES G. BARNUM

*Am. J. Obst. & Gynec.*, 50: 439-42, October, 1945

Dystocia due to the shoulders occasionally presents a serious problem. It may be due to one or more factors; with an over-sized baby the shoulders are large in proportion to the head and the anterior shoulder may impinge upon the anterior arch of the pelvis in such a manner as to offer a serious obstacle to delivery. This may occur unexpectedly when a large baby is being delivered through a slightly contracted pelvis, through which a moderate-sized baby had previously been delivered with ease. Analgesia and anesthesia add to the difficulty by preventing cooperation by the patient and minimizing the effectiveness of the natural forces.

The writer describes his procedure in such a situation: With adequate anesthesia the fetal body is allowed to rise in the mother's abdomen as far as it would. The operator's hand is introduced posteriorly, to find the posterior arm. Failing to flex the elbow, the operator's hand is advanced until the fetal wrist can be released from its position across the posterior border of the pelvic inlet. The fetal elbow is flexed and the hand swept down over the anterior chest. At this time the posterior shoulder is out, but the anterior shoulder is still engaged against the symphysis.

To release the anterior shoulder, the fetus is rotated approximately 180 degrees (with the help of an assistant), so that the shoulder which is out comes into a position just outside the symphysis. This maneuver entirely unlocks the obstruction and the remainder of the delivery is readily completed.

Subsequently, the first part of this procedure was found described by DeLee and a similar description in Titus' "The Management of Obstetric Difficulties." Both state that after delivery of the posterior shoulder the remainder of the delivery was easily accomplished. This, the author states, does not appear to always be the case, and DeLee's illustration shows the operator's hand making suprapubic pressure to force the anterior shoulder under the symphysis, which might subject the fetal thorax to severe compression. This pressure could be transmitted to the heart, leading to permanent cardiac arrest. The method of rolling the baby over on its longitudinal axis and unlocking the obstruction, avoids compression of the thorax. Since first extemporizing this procedure several years ago, the writer has used it on several occasions when commoner methods failed, and in these cases delivery was accomplished without injury to mother or child.

## A PERITONEAL STAINING TECHNIQUE FOR EXTRAPERITONEAL CESAREAN SECTION

GEORGE A. BOURGEOIS

Am. J. Obst. & Gynec., 50: 191-195, 1945.

A description is given of a peritoneal staining technique designed to facilitate dissection of the peritoneofascial flap and to aid in preventing its accidental puncture during cesarean section. The urinary bladder is emptied by catheter and refilled with about 250 cc. of 0.001 per cent phenolsulfonphthalein solution and the catheter is left in the bladder. A midline incision is made down to the transversalis fascia which is stripped by blunt dissection from the undersurface of the recti muscles. A single small premeditated opening is then made into the peritoneal cavity at the extreme upper pole of the incision. A soft rubber catheter, to which a syringe containing 5 cc. of 0.5 per cent aqueous methylene blue solution has been attached, is inserted through this opening into the peritoneal cavity toward the bladder. The bladder is then emptied and the dye injected slowly over its peritoneal surface. Simultaneous manipulation of the catheter tip through the transversalis fascia and peritoneum will bring the dye in contact with all of the future peritoneofascial flap. Overflow of dye onto extraperitoneal tissues can be prevented by having an assistant elevate the edges of the peritoneal opening. The peritoneal incision is closed by fine chromic gut. The resulting sharply demarcated blue peritoneum furnishes guides for dissection of the peritoneofascial flap.

Ten cases in which this method has been employed are reported. Incomplete staining occurred in one instance because the amount of dye was insufficient and in another because the dye was injected in the presence of a distended bladder. No maternal or fetal deaths occurred. No injury to bladder or ureters was noted. Convalescence of all patients was free of peritoneal irritation or postoperative vomiting. At follow-up examinations all uteri were well involuted and freely movable.

## THE USE OF FINE CHROMIC CATGUT FOR POSTPARTUM PERINEAL REPAIR

EDWARD G. WATERS

Am. J. Obst. & Gynec., 50: 319-25, September, 1945

The author suggests that the use of very fine chromic catgut sutures is followed by primary healing of the incised perineum. When the soft parts are neither excessively overstretched by the fetus nor damaged by instrumentation,

a nulliparous type introitus may be looked for as the end result in most parturient patients. Primary posterior colpoperineorrhaphy is designated as a good procedure to follow in multiparas with relaxed structures. These findings represent the results in the follow-up of 80 per cent of a group of 400 patients studied by the author.

The function of a suture is to obtain hemostasis and hold in opposition the divided structures sufficiently long to permit adequate wound healing before loss of effective suture strength through absorption. The most desirable suture is one which evokes the least leucocytic response and permits earliest proliferation of fibroblasts. A consideration of the available experimental data indicates the use of the smallest chromic sutures possible with due consideration of the need for initial tissue coaptation. The chromic catgut used throughout this series was No. 0000 chromic catgut, with average tensile strength of 2 pounds.

In this series, the suture material removed on the third day in experimental cases only varied from 1 pound 4 ounces to 2 pounds 8 ounces in tensile strength. An incidence of over 72 per cent of patients with no postoperative pain response is notable. Ninety-eight and eight-tenths per cent of these wounds healed by primary intention with no excessive or notable tissue disturbance.

The conviction is advanced that a consideration of the theory of wound healing involving the use of fine chromic suture material and the clinical data derived from the study of these 400 patients in whom this type of suture material was used, gives evidence to the belief that it is the proper suture material to use for postpartum perineal repairs. 5 figures.

## CONTINUOUS CAUDAL ANALGESIA IN CURETTAGE FOR ABORTION

CHARLES W. NEWTON, JR. AND GEORGE J. ANDROS

*Am. J. Obst. & Gynec.*, 50: 430-33, October, 1945.

This article deals with the attempt of the authors to decrease blood loss at the time of therapeutic abortion and curettage for incomplete abortion by the use of continuous caudal analgesia as an anesthetic method. This technique maintains tonicity of the uterine muscle and at the same time provides analgesia of the perineum, vagina and in the cervical and fundal portions of the uterus.

The technique used is based upon the method originally described by Hingston and Edwards. Preoperative medication in the form of 0.2 Gm. pentobarbital sodium (Nembutal) is administered orally approximately thirty minutes before the patient is taken to the anesthetic room. With the patient on her abdomen, the lower back is surgically prepared and draped. After local infiltration of the skin, a malleable steel needle is inserted into the sacral canal through the sacral hiatus. When it has been determined that the needle is properly placed, a test dose of 8 cc. of 1.5 per cent metycaine in Ringer's solution is injected. After a

ten-minute period of observation, and in the absence of signs of spinal anesthesia, an additional 22 cc. of the analgesic agent are injected, and the patient is placed immediately upon her back. Care must be taken to prevent displacement of the needle. The operating table is tilted into 5 degrees Trendelenburg position, the patient's feet are held upward for two or three minutes, following which the legs are suspended by stirrups in lithotomy position. After an interval of about ten minutes the level of analgesia on the abdominal skin is tested by means of a sharp needle. Blood pressure is checked at five-minute intervals during the entire procedure.

The amount of 1.5 per cent metycaine used has been relatively constant, the smallest total amount injected being 40 cc. and the largest 70 cc. The average dose has been less than 55 cc. This variance in amount necessary, to produce satisfactory analgesia is probably due to individual susceptibility to the drug and to the size of the patient. The amount must be regulated by objective and subjective findings.

In the series of 22 consecutive cases there were no anesthetic, operative or postoperative complications. Convalescence and return to normal activity of the patient is hastened.

One table; three references.

## SOCIAL AND LEGAL ASPECTS

### THE INFLUENCE OF SOCIAL AND ECONOMIC FACTORS ON STILLBIRTHS AND NEONATAL DEATHS

DUGALD BAIRD

J. Obst. & Gynaec. Brit. Emp., 52: 217-34, June, 1945

In order to compare stillbirth and neonatal mortality-rates in different social classes, the author has analysed the records of 3 groups of Aberdeen cases. Group 1 composed a series of 1, 419 delivered in a nursing home, belonging to the Registrar-General's social classes I and II (high income groups) and mostly under the care of the family doctor. Group 2 was a series of 8,808 booked hospital cases, under the care of specialists, belonging to social classes III, IV and V (low income groups). Group 3 consisted of 501 cases in private specialist practice. In the 3 groups the stillbirth-rates were 25.3, 30.4 and 10.0 respectively and the neonatal mortality 13.0, 34.5 and 8.1.

In Groups 1 and 2 the stillbirth-rates in full-time and premature infants were the same, and in each group the stillbirth-rate in premature infants was 10 times that in full-time infants. The excess mortality of Group 2 over Group 1 was due to the incidence of prematurity in Group 2 being almost double that in Group 1.

The patients in Groups 1 and 3 are in the same social class and the differences in the stillbirth- and neonatal mortality-rates are probably due to different standards of obstetric care. In Group 1 the stillbirth-rate has fallen from 47.6 in the years 1933-37, to 14.9 in the year 1944. This fall is due mainly to improved obstetrics.

In Group 2 the stillbirth-rate is 3 times that in Group 3, although the standards of obstetric care are the same. There is very little scope for reduction in the stillbirth-rate in Group 2 except by measures designed to improve the health and nutrition of the mother. The problem of the high neonatal mortality in Group 2 is largely one of the prevention of prematurity.

The stillbirth-rate is relatively high with first pregnancies, least in the second and thereafter rises with each pregnancy. The rate rises with age in each parity. In Group 2 the stillbirth-rate in the age group 25 to 34 in primiparae is nearly 5 times that in the same age group of primiparae in Group 1. The reproductive efficiency in Group 2 as measured by the stillbirth-rate falls off steadily after the age of 20, whereas in Groups 1 and 3, the fall in efficiency is delayed until the age of 30. In Group 2, 63 per cent of the primiparae are under 25 years of age and in Groups 1 and 3, 19 per cent. The stillbirth-rate in the latter groups would be very high if the reproductive efficiency in these groups fell off as quickly with age as it does in Group 2.

Over 30 per cent of the stillbirths in full-time infants in Group 2 are due to intra-uterine death of the fetus due to unexplained causes. The cause of the

onset of premature labor is unexplained in about 50 per cent of cases. The most probable explanation in both instances is poor health and nutrition of the mother.

From a national point of view, the stillbirth and neonatal mortality-rates will be lowered most substantially by improvement in the health and nutrition of the mothers in Social Classes III, IV and V, corresponding to Group 2 in this series, as they constitute the vast majority. 9 references.

## THE INFLUENCE OF SOCIAL AND ECONOMIC FACTORS ON STILLBIRTHS AND NEONATAL DEATHS

DUGALD BAIRD

J. Obst. & Gynaec. Brit. Emp., 52: 339-66, Aug., 1945

The author proposes, in this paper, to examine the probable causes of prematurity, basing the discussion on a previous paper which showed the importance of prematurity as a cause of stillbirth and neonatal mortality in Social Classes III, IV and V.

Prematurity is almost twice as high in Social Classes III, IV and V as in Classes I and II. In the former classes, 50 per cent of the prematurity is unexplained. The most common obstetrical condition associated with prematurity is eclamptic toxemia and this is twice as common among the poor as the well-to-do for the same age and parity group. Twin pregnancy is a great strain in the lower classes. The most likely explanation of these differences is that among the lower classes the health and nutrition of the mother is inferior. Variability in the incidence of prematurity within the lower classes suggests that poor health of the mother may be dependent upon growth and general nutrition in early years rather than on the diet during pregnancy.

In the pre-war years it has been shown by Orr and others that as the income rises, the amount spent on food increases and the diet improves. Fifty per cent of the population has a diet inadequate for full health. This 50 per cent contains about two-thirds of the children. As income increases, disease and death rate decrease, children grow more quickly, adult stature is greater and general health and physique improve.

A study was made of the heights of expectant mothers and of the weights of their babies with results showing that the weight of the baby increases with the height of the mother. If a mother does not grow to full height, her pelvis is unlikely to develop fully. The danger of this would be increased if the mother's nutrition during pregnancy were good and a large baby produced. The incidence of rickets is high in association with general poor health and physique and also in association with high stillbirth-rates.

A study of diets of 300 women was made as follows: 100 mothers with stillborn

infants; 100 mothers with premature born infants; and 100 mothers of full-time infants. The average daily caloric intakes in these groups were 1,644, 1,710 and 1,946 respectively. The diet of the mothers of full-time infants was superior in every respect.

From a study of the stillbirth and neonatal mortality-rates during the war years, it can be inferred that the war has improved the social position of Classes III, IV and V, in so far as it affects women in these classes having fewer stillbirths and deaths in the first 3 days of life from prematurity and "unknown causes." Improved nutrition during pregnancy seems to be the most likely explanation.

In 1940 and 1941 there was a sharp fall in food supplies and at the same time a rise in neonatal mortality due to infection. In 1942 figures show an improvement in food supplies largely resulting from Lend-Lease supplies and from then on the supplies have remained fairly constant. Since the war, unemployment has disappeared and wages are higher. In 1943 there was an 80 per cent increase in the consumption of liquid milk in the working classes.

The stillbirth-rate has been falling fairly steadily throughout the war years in Scotland, England and Wales, while that part of neonatal mortality due to prematurity, congenital debility and birth injury has fallen markedly since 1942. 19 references.

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# Maternal Mortality Reports

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*(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.*

*Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)*

## CASE NO. 1

The patient was a twenty-seven year old colored multigravida, who was admitted to the hospital on June 21 at 1:45 A.M. with a history of having had three generalized convulsions prior to admission. The E. D. C. was the latter part of August. She was first seen on March 15, at which time her blood pressure was 130/65, her weight 98 pounds and she was thought to be twenty to twenty-two weeks pregnant. She was observed on four subsequent occasions, the last time being on May 31. At that time the blood pressure was 114/78; the weight 114 pounds, and she was instructed to return on June 21. On June 20, however, she visited the office about noon complaining of intermittent abdominal pain and it was thought that she was probably in premature labor. On examination the presenting part was floating and the cervix was not effaced and not dilated. She presented no apparent signs that the examiner recognized as indicative of toxemia. *Her blood pressure was not taken and her urine was not examined.* She was told that she was not in labor and could go home.

She was next seen approximately twelve hours later in the hospital. The history obtained at that time was that she had had three generalized convulsions during which she chewed her tongue, and following which there was loss of vision. On admission her blood pressure was 220/140. The fundus was 23 centimeters above the symphysis and the fetal heart could not be heard. There was a small amount of ankle edema and the patient was comatose. The temperature was 101° rectally, the pulse rate 96 per minute and the respirations 24. A catheterized specimen of urine revealed four plus albumin. Treatment was begun immediately. Sedation and digitalization, accompanied by the administration of considerable quantities of glucose, were carried out. Her blood pressure readings remained at a high level for the first twenty-four hours of hospitalization, and then began to drop reaching a low point of 135/104 at 4:00 A.M. on June 22. Continuous oxygen by mask was being given and it was frequently necessary to remove mucus and vomitus from the mouth and throat by suction. Ophthalmoscopic examination revealed small hemorrhages in both fundi and evidences of hypertensive retinitis. The patient's condition remained critical throughout the 23rd and 24th of June. At 3:42 A.M. on June 25 she was delivered spontaneously of a 30 week dead macerated child weighing 2 pounds 12 ounces. She seemed to improve somewhat for a few hours, but on the morning of the 26th she lapsed into a coma, her pulse became weak and at times imperceptible, and her respirations markedly increased. Plasma, whole blood, and glucose were given but no improvement resulted. Every manner of supportive therapy was attempted with little result and on July 1 respirations ceased.

*Discussion:* The value of adequate prenatal care as a means for the prevention of eclampsia has been amply demonstrated in the experience of everyone concerned with the care of the pregnant female. This basic principle of maternal

care needs no additional substantiating proof here. Registration early in pregnancy with complete physical examination followed by adequate observation throughout pregnancy is an essential part of good care. The failure to take this patient's blood pressure when she was seen prior to the onset of the eclamptic convulsions was inexcusable, and probably played a large part in the result in this case. Adequate treatment at that time might have avoided the convulsions and the subsequent fatality. This death must be judged as a preventable one.

#### CASE NO. 2

The patient was a thirty-six year old white multigravida, IV, who was admitted to the hospital on February 14. According to the history given by the patient, she had been under the care of a midwife and had an entirely uneventful prenatal course except for some slight ankle edema during the last three weeks. At no time had she been seen by a physician prior to admission to the hospital. She began to have labor pains at noon on February 13 and sent for the midwife. After seven hours of poor pains no progress seems to have been made. During that period frequent and repeated non-sterile vaginal examinations were carried out by the midwife. No history could be elicited of the administration of any oxytocics.

Early on the morning of February 14 the midwife sent for a physician, who after a physical examination, including a rectal examination, sent the patient to the hospital. On admission to the hospital the patient's temperature was 96°F.; the pulse rate 168 per minute, the blood pressure 130/100, and the fetal heart was not audible. Upon examination the patient was found to have a frank breech presentation, the presenting part being at the level of the spines, and the cervix fully dilated. There was no bleeding apparent. The patient was catheterized and about 15 cc. of gross blood was obtained. Contractions of the uterus were noted at this time which were of slight intensity and very irregular. X-ray examination confirmed the presentation of the fetus.

Further examination of the patient established a diagnosis of a rupture of the uterus and the patient was taken to the operating room. Four hours after admission the abdomen was opened under ether anesthesia and a classical cesarean section performed. The child was stillborn. There was no free blood in the peritoneum, but upon examination a tear was found in the right lateral wall of the uterus extending from the region of the cervix to the cornu. The right broad ligament was markedly infiltrated with old blood clots. An hysterectomy and a right salpingo-oophorectomy were performed and a drain placed through the cervical stump. During the operation 450 cc. of blood and glucose were given the patient and she left the operating room in fair condition with a blood pressure of 120/90 and a pulse rate of 160 per minute.

Due to the foul odor of the uterine contents found at operation, sulfa therapy was started immediately and 1000 cc. of citrated blood were given late that evening. The patient appeared to rally satisfactorily. Fluids were taken fairly well and the urinary output was good. On February 15 another 500 cc. of citrated blood was given. However, on February 16 the patient became increasingly drowsy and finally lapsed into coma. Her downhill course was rapid and respirations ceased at 4:45 A.M. on February 17.

Postmortem examination was refused but from the clinical picture it was thought that the patient died of an overwhelming infection.

*Discussion:* The repeated vaginal "examinations" by the midwife doubtless entailed efforts to manipulate the breech and were probably the immediate cause of the rupture. The fact that they were unsterile contributed also to the fatal outcome in as much as the terminal picture was one of generalized infection. It is reprehensible that this type of midwife should be allowed to practice at all, let alone manage breech deliveries. The Committee feels that these untrained,

"Granny" midwives must be eliminated entirely and replaced either by physicians or by supervised nurse-midwives if the high maternal mortality rates in certain areas are to be lowered.

Upon admission to the hospital the rapid pulse, the bloody urine and the absent fetal heart indicated that rupture had already taken place. Why, then, did four hours intervene between admission and operation? Although this obviously preventable death is primarily chargeable to the midwife, prompt operation might have saved the patient.

### CASE NO. 3

This patient was a seventeen year old white primigravida who was admitted to the hospital on June 23 at 5:25 P.M. She was in active labor, and her temperature, pulse and respirations were normal. The blood pressure was 120/80. Her last menstrual period was September 12 and the estimated date of confinement was June 19. Her labor pains began on June 23 at 5:00 P.M. On June 24 at 4:15 A.M. the patient was given 50 mg. of Demoral by mouth. At this time the cervix was 6 centimeters dilated and the presenting part was in low pelvis. At 12:10 P.M. the patient was taken to the delivery room and prepared for delivery. Under sterile technique, a vaginal examination revealed the cervix to be almost fully dilated. The patient was given two minims of pitocin intramuscularly and the membranes were artificially ruptured. At this examination the head was found to be in low-mid pelvis. At 12:30 P.M. forceps were applied to the presenting part and a right-occipito-transverse was rotated with the forceps to an anterior position. At 1:04 P.M. a full term living male child weighing 7 pounds 3 ounces was delivered by forceps extraction under ether anesthesia. A first degree laceration was immediately repaired. There was no abnormal bleeding at this time and at 1:15 P.M. the placenta and membranes were expressed intact. The patient was given one ampule of pitocin intramuscularly and an ampule of ergotrate intravenously at this time. The uterus however did not seem to remain firm in spite of vigorous and continuous massage through the abdominal wall. The bleeding continued rather freely in spite of another ampule of ergotrate by vein. The situation became alarming and it was decided to pack the uterus. At 1:30 P.M. one uterine pack was inserted. At 2:00 P.M. her blood pressure was thought to be 42 mm. of mercury systolic. Five hundred cubic centimeters of ten per cent glucose was started intravenously and five hundred cubic centimeters of normal saline was given by hypodermoclysis. At 2:12 P.M. morphine sulphate grains  $\frac{1}{4}$  and atropine sulphate grains  $\frac{1}{16}$  were given. At 2:20 P.M. five hundred cubic centimeters of blood plasma were rapidly administered and another five hundred cubic centimeters of ten per cent glucose was begun. The patient was given oxygen by mask. At this time she was very restless and quite noisy. The uterus repeatedly relaxed as soon as active massage was stopped. At 2:30 P.M. the pulse and blood pressure were unobtainable and at this time the injection of five hundred cubic centimeters of citrated blood was begun. One ampule of ephedrine sulphate and more pitocin were given the patient between 2:30 P.M. and 2:45 P.M.

At this time the Obstetrical Resident removed the uterine pack and examined the patient carefully by vagina. There was no evidence of an inversion of the uterus, but a small cervical laceration at three o'clock was found. The uterus was then packed tightly with three large gauze packs soaked in bichloride of mercury solution. At this time the radial pulse was unobtainable and the respirations were quite shallow and rapid. At 3:00 P.M. respirations stopped completely; however the use of adrenaline and artificial respiration served to reestablish breathing. The patient's condition was critical, and in spite of stimulants and the use of a respirator, she was pronounced dead at 3:40 P.M.

*Discussion:* What was the hurry in this case? The fact that the patient was taken to the delivery room and prepared for delivery seems to have been taken as

an indication for prompt action, despite the fact that the cervix was not yet fully dilated. Between "almost fully dilated" and "fully dilated" there is a great gulf of difficulty. It would have been immeasurably better obstetrics to have removed the drapes and given this patient an hour or more of labor. In all likelihood this would have resulted very shortly in a completely dilated cervix and a head which was on the perineum, in sight and in occiput-anterior position. An easy outlet forceps would then have been possible.

Instead, two minims of pituitrin were given, the membranes were artificially ruptured and after twenty minutes forceps were applied when the head was still in "low mid-pelvis" and had not yet rotated. There was no indication for this interference. That it was not an easy forceps operation is shown by the fact that it required 34 minutes for delivery.

The Committee suspects that the unnecessary haste in effecting this delivery caused: (1) unrecognized injury to the cervix and lower uterine segment in addition to the small tear which was observed; and (2) uterine relaxation because of the prolonged anesthesia necessary. It feels, moreover, that no death in which pituitrin is given prior to the birth of the infant can be written off as non-preventable unless proof positive can be adduced to rule out uterine rupture and cervical tears. The extreme rapidity with which this patient died suggests rupture in this case.

The use of pituitrin in this case plus the unjustified forceps operation seemed to the Committee reprehensible as were also the inadequate amount of blood given the patient and the use of uterine pack soaked with bichloride of mercury. It was classified as a preventable death.

#### CASE NO. 4

The patient was a 28 year old colored multigravida, (V) who was admitted to the hospital on October 8, not in labor, and with a diagnosis of an upper respiratory infection and the possibility of cardiac decompensation. Her past history revealed that she had a syphilitic infection for which she had been receiving wholly inadequate treatment. The last menstrual period was on February 9 and the estimated date of confinement November 16.

On admission to the hospital, the patient's temperature was 100.2°F., her pulse rate 98 and respirations 34 per minute. She complained of pain in her chest and shortness of breath. The blood pressure was 130/70. She was seen by a competent medical consultant shortly after admission to the hospital and it was his impression that there was an acute upper respiratory infection present, mitral and aortic heart disease, and unmistakable evidences of cardiac failure. Digitalization and a decreased fluid intake were immediately ordered.

Careful study of the prenatal record of this patient revealed that in May she had been examined by a cardiologist because of the presence of a heart murmur, but the suspected aortic valvular disease was diagnosed at that time as "purely functional with no evidence of heart disease." On admission to the hospital the duration of pregnancy was about 34 weeks. An x-ray on this day revealed no pulmonary pathology.

The patient's course was uneventful for the first twenty-four hours of hospitalization except for frequent coughing. The temperature varied between 99.2°F. and 100.8°F., the pulse rate varied between 92 and 120 per minute, and the respirations between 24 and 40. On October 9 at approximately 8:28 P.M., the patient went into labor spontaneously, and after a total labor of four hours and twenty-five minutes she was delivered without anesthesia by breech extraction of a slightly premature living child in good condition. The

third stage was uneventful and there was no abnormal amount of bleeding. The time of delivery was 2:18 A.M. on October 10. Following delivery she was given pitocin, ergotrate, and  $\frac{1}{2}$  grain of pantopon. At this time her condition seemed to be satisfactory. The pulse rate was 108 per minute and the respirations 26. At about 3:00 A.M. however it was discovered that the patient was markedly dyspneic, her pulse rapid and weak, and the blood pressure unobtainable. Immediately following delivery it was 98/58. The patient was in great respiratory distress at this time, and the radial pulse rapidly became imperceptible. The lung fields revealed palpable rhonchi and audible inspiratory and expiratory rales over the entire anterior and axillary areas. Tourniquets were applied to all four extremities, oxygen was given by mask, and 50 cc. of 50 per cent glucose was administered. Morphine sulphate grains  $\frac{1}{4}$ , aminophyllin and strophanthin were given but to no avail. Respirations became more and more labored and increasingly slow. The patient's condition grew worse rapidly and at 4:23 A.M. on October 10 she expired. No autopsy was obtained.

*Discussion:* The early recognition and appropriate treatment of organic heart disease complicated by pregnancy are essential if the number of deaths associated with this condition are to be decreased. The classification of heart disease on a functional basis by the New York Heart Association is based upon an estimation of cardiac capacity derived from the patient's history of past and present disability. Recommendations for the treatment of pregnant women with heart disease based upon this functional classification have greatly reduced the fatalities from this serious complication. Almost one-tenth of all deaths from puerperal causes are caused by heart disease.

In this patient the heart disease was not recognized early in pregnancy and as a result proper treatment was impossible. Hence, the death was classified as preventable. Restriction of physical activity during pregnancy even to the extent of complete bed rest for many weeks when indicated, frequently spells the difference between life and death for the patient. The proper conduct of labor, the appropriate method of delivery and the intelligent choice of anesthetic are most important.

The death of the cardiac patient in the first twenty-four or forty-eight hours following delivery is not unusual, and in every patient with heart disease it is important to watch her most closely following delivery. The frequency of avoidable maternal deaths from this cause should warn us of the seriousness of this condition and keep us on the alert for its recognition and appropriate treatment.

#### CASE NO. 5

The patient was a fifteen year old white primigravida who was admitted to the hospital on February 12 in active labor. The last menstrual period was in June and the estimated date of confinement in February. Her prenatal course had been negative except for slight edema of the ankles and an elevation of blood pressure up to 145/90 of one week's duration.

Labor pains began on February 12 at 2:00 A.M., twelve hours prior to admission to the hospital. The past history and family history were negative. Examination on admission revealed a full term fetus lying in an L.O.T. position, estimated weight of the fetus approximately seven pounds. The blood pressure was 135/90. There was a one to two plus pitting edema of the lower extremities. The heart was questionably enlarged to the left and tubular breath sounds were thought to be heard over the left upper chest posteriorly. The examination of the urine was negative. Rectal examination showed the cervix to be five cms. dilated, the membranes intact, and the presenting part level with the spines.

Following admission labor progressed normally, and at 1:30 P.M. the patient was given nembutal grains 3. No other medication except Vitamin K was given. At 2:30 P.M. the membranes ruptured spontaneously. At this time the cervix was fully dilated and the presenting part was 3 cms. below the spines. Her blood pressure was 135/90.

The patient was taken to the delivery room, prepared for delivery and at 2:47 P.M. nitrous oxide and oxygen anesthesia was begun. Approximately fifteen minutes later the anesthetic mixture was changed to ether-oxygen. Examination revealed the cervix to be fully dilated and the presenting part on the perineum. At 3:25 P.M. a full term living male child weighing 7 pounds 8 ounces was delivered by low forceps following a central episiotomy. The baby cried spontaneously requiring no resuscitation. At 3:37 P.M., the placenta and membranes were expressed intact.

Inspection of the vagina and cervix revealed no lacerations. The total length of labor was 13 hours and 47 minutes. The total blood loss was estimated to be about 400 cubic centimeters. At 3:45 P.M. the repair of the episiotomy was begun. At 4:00 P.M. it was noticed that the patient was extremely cyanotic and that she was breathing very poorly. Metrazol, caffeine-sodium-henzoate, intracardiac adrenalin, artificial respiration and intratracheal oxygen were of no avail and the patient was pronounced dead at 4:05 P.M. Post-mortem examination revealed atelectasis of the lower lobes of both lungs and fatty changes in the liver.

The anesthetic was given by an intern on the obstetrical house staff. Everyone present at the time of this patient's death was of the opinion that this was undoubtedly an anesthetic death of unknown etiology.

*Discussion:* The universal use of properly selected anesthetics of proved safety administered by adequately trained anesthetists could be the means of saving the lives of a considerable number of pregnant women annually in the United States. No single analgesic or anesthetic is entirely satisfactory for all patients during labor. Analgesia prolongs labor and increases fetal and maternal mortality, and accordingly must be used cautiously and intelligently. The responsibility of the obstetrician is primarily to insure a living mother and baby. The alleviation of pain at a cost of the mother or the child must be avoided in spite of any vociferous demands of the lay public which is in no position to estimate the part played by the increased use of analgesia and anesthesia as a cause of many preventable deaths.

The cause of death in this particular case was a most unique one and was only discovered many hours after this patient's death. The oxygen tank was connected to the nitrous oxide valve and the nitrous oxide tank was connected to the oxygen valve. Ether and nitrous oxide were being given in error instead of oxygen. What price anesthesia!

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# Gynecology

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## ENDOCRINOLOGY

### TREATMENT OF HYPOOVARIANISM BY THE SEQUENTIAL AND CYCLIC ADMINISTRATION OF EQUINE AND CHORIONIC GONADOTROPINS—SO-CALLED ONE-TWO CYCLIC GONADOTROPIC THERAPY. SUMMARY OF FIVE YEARS' RESULTS

E. C. HAMBLÉN AND C. D. DAVIS

Am. J. Obst. & Gynec., 50: 137-146, 1945

This article brings up to date the results of a series of experiments on treatment by the sequential or cyclic administration of equine or chorionic gonadotropins begun in 1939 and reported upon in the October, 1940, and March, 1941, issues of the same journal. In all, 116 patients with hypofunctioning ovaries were studied. The clinical studies of all the patients included endocrine and gynecological surveys, determinations of basal metabolic rates, roentgenograms of the sella turcica and, in patients with deficient sexual maturation and those under 20 years of age, roentgenological estimations of osseous age. Special methods of study and of handling of the patients in the four clinical categories are described in detail. The first group included seven patients with deficient sexual maturation and non-occurrence of menarche. Only one of these yielded a progestational endometrium during one-two cyclic gonatropic therapy. Group 2 was comprised of 13 patients with infrequent and/or scanty bleeding. Four (30.5 per cent) yielded progestational endometrium during therapy. Fifteen (48.5 per cent) of the 31 patients in group 3 with prolonged and/or excessive estrogenic bleeding yielded progestational endometrium during therapy. Seven of the 14 patients with prolonged and/or excessive estrogenic bleeding (group 4a) yielded positive responses, including four pregnancies, during therapy, and 9 of 50 patients with cyclic bleeding from immature progestational endometrium (group 4b) became pregnant during therapy. It is concluded that patients with hypoenestrogenism (as illustrated by group 1) respond poorly to this system of gonadotropic therapy, whereas those with anovulatory failure without hypoenestrogenism (groups 2-4) respond well.

(See also comment on following abstract of a paper by the same authors. In the present paper, the results reported will not fill anyone with enthusiasm concerning the results of organotherapy in spite of the apparently fair results in the small group of anovulatory cases included in the authors' series. This is no reflection on the authors or the plan of gonado-

tropic therapy they describe, because the results by any other plan are just as unfavorable. In this field of organotherapy, as in so many others, we are still in the floundering stage.—Ed.)

## A COMPARATIVE STUDY OF THE CLINICAL RESPONSES OF WOMEN WITH HYPOFUNCTIONING OVARIES TO TWO METHODS OF COMBINED GONADOTROPIC THERAPY

C. D. DAVIS AND E. C. HAMBLEN

*Am. J. Obst. & Gynec.*, 50: 269-74, September, 1945

The authors found, in a previous study, that the sequential and cyclic administration of equine and chorionic gonadotropins (one-two cyclic gonadotropin therapy) restored to a fertile status a number of women with hypofunctioning ovaries. Believing that the commercial product containing both pituitary synergist and chorionic gonadotropin might yield as effective therapy as the former, they made a comparative study of the two types of treatment in a group of twenty-one patients.

These patients fell into four clinical categories: (1) four patients with deficient sexual maturation in whom the menarche had not occurred; (2) six patients with infrequent and/or scanty estrogenic bleeding; (3) five patients with prolonged and/or excessive estrogenic bleeding; and (4) six patients with presumed ovarian sterility associated with bleeding from immature progesterational endometria.

The two methods of treatment, single and sequential administration of equine and chorionic gonadotropins and administration of a mixture of pituitary synergist and chorionic gonadotropin (hereafter called SYN.), were employed. Positive responses followed the latter therapy only when it was given for 20 days, from the fifth through the twenty-fourth days of the cycle. The primary criterion for an evaluation of these responses was a study of endometrial biopsies taken prior to and following treatment.

No patient gave any evidence that her ovaries were stimulated to full physiologic activity. None of the patients with deficient sexual maturation responded to either therapy. Patients with infrequent and/or scanty estrogenic bleeding and those with prolonged and/or excessive estrogenic bleeding responded to both therapies. The more positive responses were associated with one-two cyclic gonadotropic therapy. No pregnancies were associated with either therapy in the group of patients with presumed ovarian sterility. However, it is the opinion of the authors that when a larger series of patients with sterility are treated with SYN., pregnancies may be obtained. Despite negative skin tests, 3 of the 21 patients experienced rather severe local and constitutional reactions.

Cyclic therapy with SYN. may produce progesterational endometria in patients experiencing various grades of estrogenic bleeding. It is apparent, however, that when these two groups of patients are considered, the use of SYN. therapy, although producing favorable responses, does not afford as high an

incidence of these responses as the single and sequential administration of equine and chorionic gonadotropins. 6 references.

(The number of cases on which this comparative study was based is a rather small one, and the results in this small group would not seem to warrant any very decisive conclusions as to the relative efficacy of the two plans of treatment discussed in the paper. Furthermore, the results obtained by both methods appear rather unimpressive. The experimental work of Evans and others certainly justifies the opinion that a pituitary synergistic factor is of importance in the still rather obscure field of hypophysio-gonadal interrelationships, and there is circumstantial evidence along this line in some of the human endocrinopathies involving these two glands, especially in pregnant women.

Since the over-enthusiastic report of Davis and Koff some years ago as to the supposed value of equine gonadotropin as a stimulant of human ovulation, followed by a wild wave of such gonadotropic therapy in the treatment of sterility, more and more evidence has accumulated to indicate that the equine and other gonadotropins have very little effect upon the human ovary, and certainly no critical observer has published any worthwhile evidence of their clinical value. One always feels like apologizing for making such destructive criticisms, since it does not seem possible to recommend any other plan of treatment which would be any more effective or logical.

Certainly the comparative study reported in this paper for the four indications enumerated therein is a laudable one, and it is hoped that it will be extended to a larger group of patients. The commercial synergistic preparation which the authors designate as SYN is obviously synapoidin. A hazard which many have emphasized in connection with the use of this preparation is that it may produce even rather large cysts of the ovary. While these may be only transitory, they are certainly undesirable, and the substance should be employed with caution, avoiding too large dosage or too prolonged administration.—Ed.)

## STUDIES IN AMENORRHEA, OLIGOMENORRHEA, AND ANOVULOMENORRHEA. I. EFFECT OF EQUINE GONADOTROPHIN UPON ESTABLISHMENT OF CYCLIC MENSES AND OVULATION

A. R. ABARBANEL AND J. H. LEATHEM

*Am. J. Obst. & Gynec.*, 50: 262-69, September, 1945

A gonadotrophin isolated from the serum of the pregnant mare, known as equine gonadotrophin, recently has received attention from the medical profession for the treatment of the clinically hypofunctioning ovary.

In this report, the author discusses results from the use of equine gonadotrophin in treating 22 patients. Of these, 3 had primary amenorrhea, 11 had secondary amenorrhea, 7 had oligomenorrhea and one had regular anovulomenorrhea.

Pretreatment data included endometrial biopsies, determinations of basal metabolic rates, red cell counts and hemoglobin, routine urinalysis and, where indicated, x-ray studies of chest and bone. If the regular menses did not appear after an observation period of from 3 to 9 months, adjuvant therapy with equine gonadotrophin was instituted. Each course of equine gonadotrophin was given over a seven to ten day period.

The effects of equine gonadotrophin on these four conditions were as follows: the hormone failed to establish menses in the 3 cases of primary amenorrhea; of the 11 cases of secondary amenorrhea, ovulation was apparently stimulated in 2, although one case was open to serious question; in the 7 cases of oligomenorrhea, equine gonadotrophin apparently restored cyclic menses in one but failed to stimulate ovulatory response in any; equine gonadotrophin was ineffectual in the one case of regular anovulomenorrhea. Nine of these patients later were salvaged with an adequate diet and, usually, thyroid extract.

There proved to be possible harmful effects in the administration of equine gonadotrophin including a gonadotoxic effect on the ovary, development of antagonistic substances with neutralization of subsequent injections of the hormone, and development of allergic manifestations, in spite of negative skin tests.

It seems like more rational therapy to influence the clinically hypofunctioning ovary by means of its normal regulator, the anterior pituitary, by means of a nutritionally balanced diet and the thyroid hormone than by the use of substitute heterogeneous gonadotrophins whose value as yet is unproved and whose effects at best are temporary and may be even gonadotoxic. 15 references.

(The study of this small group of patients, yielding almost negative results from the employment of equine gonadotrophin in the various ovarian deficiency disorders, can be added to similarly unfavorable reports by various other observers. It would seem probable that the enormous sales which must formerly have been made of commercial preparations of the equine gonadotrophes must have undergone considerable shrinkage during the past two or three years. While not exactly comparable, it would be well to refer the reader to the abstracts in this issue of papers by Hamblen and Davis.—Ed.)

## HORMONAL INDUCTION OF MATING RESPONSES IN A RAT WITH CONGENITAL ABSENCE OF GONADAL TISSUE

FRANK A. BEACH

Anat. Rec., 92: 289-292, 1945

The case is reported of a virgin female rat, between 90 and 100 days of age, in which examination for spaying disclosed the absence of uterine horns and unruptured external vagina. Later, at autopsy, no trace of gonadal tissue nor masses of fatty tissue normally associated with the ovarian capsule and the uterine horns were found. The vagina entered a short, abortive, uterine-like structure, 8 mm. long, which ended blindly at about the point where bifurcation would normally occur. An intramuscular injection of 500 R.U. of estradiol benzoate was followed after a 48-hour interval by the injection of 0.5 mg. of progesterone. When placed with a male 12 hours later, this rat displayed all elements of the mating pattern shown by a female in normal estrus.

From the record of this animal's behavior the author concludes that it appears that differentiation and development of the neural structures controlling sexual

behavior occurred in this case despite the absence of any gonadal hormones. It is proposed that the ontogenetic development of these mechanisms is inherent in the chromosomal constitution of the genetically determined sex of the organism, and that insofar as overt behavior is concerned, the gonadal hormones may not come into play until, just before maturity, they reach a concentration sufficient to alter the sensitivity of the pre-organized neural mechanisms, and markedly increase the responsiveness of the latter to exteroceptive stimulation.

## SYNTHETIC OESTROGENS IN CANCER

E. C. Dodds

Biochem. J., 39: i-ii, 1945

The synthetic estrogens are considered as belonging to two groups: (a) derivatives of normal hexane (hexestrol, stilbestrol, dienestrol) and (b) derivatives of ethylene (triphenyl ethylene and its derivatives). Those of group (a) possess greater activity than the naturally occurring hormones, while those of group (b) are many times weaker. Those of group (a) are all highly active by mouth. A brief review is given of the results of some of the work with this group of compounds in relation to cancer. The first evidence that they could play a part in the treatment of cancer arose from observations on carcinoma of the prostate. The great majority of the patients who had been given synthetic estrogens by mouth showed complete relief of symptoms and could be maintained symptom-free for long periods.

The mode of action is still obscure, but three possibilities are presented: (1) inhibition of testosterone secretion by the testis; (2) inhibition of secretion of gonadotrophin by the anterior lobe of the pituitary; (3) direct action on the growth. It is as yet impossible to assign the relative importance of these three possible factors, but the fact that compounds of such widely differing chemical structure as estradiol and stilbestrol are both capable of causing symptomatic relief, points to the activity lying in their estrogenic activity rather than their chemical structure.

Empirical use has been made of this type of treatment in every type of cancer, but the reported results are of doubtful value. There does, however, appear to emerge the idea that favorable results may be obtained in a very limited percentage of cases of carcinoma of the breast.

(A sane and conservative presentation by the leader of the group of British physiologists who "discovered" the estrogenic potency of the non-hormonal stilbene group of substances, notably diethylstilbestrol. Would that all the stilbestrol disciples were equally conservative! —Ed.)

The effects of equine gonadotrophin on these four conditions were as follows: the hormone failed to establish menses in the 3 cases of primary amenorrhea; of the 11 cases of secondary amenorrhea, ovulation was apparently stimulated in 2, although one case was open to serious question; in the 7 cases of oligomenorrhea, equine gonadotrophin apparently restored cyclic menses in one but failed to stimulate ovulatory response in any; equine gonadotrophin was ineffectual in the one case of regular anovulomenorrhea. Nine of these patients later were salvaged with an adequate diet and, usually, thyroid extract.

There proved to be possible harmful effects in the administration of equine gonadotrophin including a gonadotoxic effect on the ovary, development of antagonistic substances with neutralization of subsequent injections of the hormone, and development of allergic manifestations, in spite of negative skin tests.

It seems like more rational therapy to influence the clinically hypofunctioning ovary by means of its normal regulator, the anterior pituitary, by means of a nutritionally balanced diet and the thyroid hormone than by the use of substitute heterogeneous gonadotrophins whose value as yet is unproved and whose effects at best are temporary and may be even gonadotoxic. 15 references.

(The study of this small group of patients, yielding almost negative results from the employment of equine gonadotrophin in the various ovarian deficiency disorders, can be added to similarly unfavorable reports by various other observers. It would seem probable that the enormous sales which must formerly have been made of commercial preparations of the equine gonadotrophes must have undergone considerable shrinkage during the past two or three years. While not exactly comparable, it would be well to refer the reader to the abstracts in this issue of papers by Hamblen and Davis.—Ed.)

## HORMONAL INDUCTION OF MATING RESPONSES IN A RAT WITH CONGENITAL ABSENCE OF GONADAL TISSUE

FRANK A. BEACH

Anat. Rec., 92: 289-292, 1945

The case is reported of a virgin female rat, between 90 and 100 days of age, in which examination for spaying disclosed the absence of uterine horns and unruptured external vagina. Later, at autopsy, no trace of gonadal tissue nor masses of fatty tissue normally associated with the ovarian capsule and the uterine horns were found. The vagina entered a short, abortive, uterine-like structure, 8 mm. long, which ended blindly at about the point where bifurcation would normally occur. An intramuscular injection of 500 R.U. of estradiol benzoate was followed after a 48-hour interval by the injection of 0.5 mg. of progesterone. When placed with a male 12 hours later, this rat displayed all elements of the mating pattern shown by a female in normal estrus.

From the record of this animal's behavior the author concludes that it appears that differentiation and development of the neural structures controlling sexual

## A NEW TEST FOR BLOOD ESTROGEN

CARL G. HARTMAN AND J. LITRELL

Science, 102: 178-179, 1945

The test described is based on the fact that the vagina of the rat remains closed until sexual maturity but opens earlier in response to the administration of estrogens. A 0.01 to 0.02 cc. sample is injected subcutaneously near the region of the future vaginal orifice. Observations are made once daily. On the average, four to five days are required for the vagina to open. However, the first indication of a positive reaction, a crescent-shaped transverse dimpling of the skin at the developing vaginal orifice, is easily recognizable within 24 hours. Usually 21-day-old female rats were employed, but six 16-day-old rats were used successfully. The test was sensitive to blood estrogens in amounts as small as 0.02 cc. of untreated finger blood from a woman in the middle of her menstrual cycle. Bloods from four different men were always negative. The authors point out that the test costs little, for the animals are not sacrificed, and that the time required to make and read the test is almost negligible.

THE EFFECTS OF THE INJECTION OF HUMAN SEMEN  
INTO FEMALE ANIMALS

P. BACSICH, A. SHARMAN AND G. M. WYBURN

J. Obst. &amp; Gynee., 52: 334-38, August, 1945

There has been some suspicion that semen may have functions other than fertilization and may contain substances which would have a beneficial action on the female genital organs. In view of the far-reaching biological and sociological implications of such a possibility, the authors performed experiments by injecting semen and testosterone propionate into animals. From the results, they conclude that semen has no gonadotrophic action.

A series of injections of human semen were given to immature rats and rabbits. There was no vaginal reaction, no evidence of estrogenic or progestational change of the uterus and no ovarian stimulation.

Injections of human semen were given to immature guinea pigs. There was no vaginal reaction and no evidence of ovarian stimulation. On the average there was a slight uterine hypertrophy but this was not regarded as significant. Injections of testosterone propionate were given to immature guinea pigs. In all the animals there was, during treatment, hypertrophy of the clitoris and in 2 guinea pigs the vaginae opened and diestrous smears were obtained. There was uterine enlargement, more marked than in the semen-treated guinea pigs, but far short of the response of the immature uterus to estrogenic therapy. There were a greater number of atretic follicles in the ovaries.

From these experiments, the authors conclude that semen does not possess the biological qualities of testosterone, nor is it probable that testosterone could be entrusted to ensure uterine maturation. 17 figures. 16 references.

(As the authors state, it has from time to time been suggested that absorption of semen might have some beneficial, possibly endocrine, effect upon the female genital organs. An ardent early advocate of this idea, Kohlbrugge (1909-10), even suggested that this constant absorption of her husband's sperm might explain why in the course of many years of married life a woman is supposed to become more and more like her husband. The older readers will remember also the discussions of an earlier day on the subject of "telegony," according to which, as Hartman defines it, "the offspring resemble not the father but an early mate of the mother either in physiological or, more commonly, pathological peculiarities. Thus, for example, a woman has a son with hypospadias by a husband with hypospadias. Her second husband is normal yet she has sons by him who also have hypospadias." This was explained by the assumption that the first husband infected the germ.

The studies reported in the present paper are of course on a properly scientific plain, and it is of interest to note that semen was found to have no testosterone-like effect. To revert for a moment to the possibility of actually harmful effects from semen absorption, the old question of spermatotoxins can not yet be completely set aside. Its application in recent years has been in the broad field of hormonal sterilization, since there were some who hoped that temporary sterility might be made possible by the injection of sperm material. Like other methods of hormonal sterilization which have been suggested and tried, the sperm injection experiments which have been done by various observers have yielded no results.—Ed.)

accepted viewpoint as to the ovulation span. The author himself states, for example, that regardless of the length of the cycle, the temperature shift occurs approximately 14 days before menstruation, as Ogino and others have urged for many years.

Granted that the exact date can be determined by the careful application of the basal temperature method, one must decide for himself if this extra information offers sufficient advantage over the simple plan of advising that coitus take place frequently during the comparatively short span of the optimum period. It must be remembered, in making such a decision, that the ovum is believed to retain its fertilizability for a good many hours, perhaps as much as 24, and that the spermatozoan is believed to maintain its fertilizing potency for at least 30 hours. It should also be remembered that the method is far more valuable in the intelligent type of patient, such as those reported by Tompkins, than in those of less intelligent type, and that definite possibilities of errors in interpretation exist, as Tompkins and others have emphasized.

It is still too early to predict whether the method will gradually achieve wide adoption, or whether it will gradually die a natural death, and this is said in no disparaging way. Perhaps a good compromise plan would be to recommend this diagnostic aid in those women whose intelligent cooperation can be assumed, while for others the customary advice as to the optimum time for fertilization might be considered to suffice.—Ed.)

## INTERPRÉTATION DES CYCLES DITS "ANOVULAIRES" CHEZ LA FEMME

G. DUBREUIL

Gynec. et Obst., Paris, 44: 61-65, 1944-45

A systematic examination of 450 ovaries of women in the reproductive period led the author to the conclusion that the so-called anovulatory cycles are in reality "progestative." The following case is cited as an example. A pregnancy terminated by delivery in September, 1943. The first cycle began in December and terminated January 6th. The second cycle was interrupted on the fourteenth day by a subtotal hysterectomy for myoma. The two intact ovaries were examined and, in addition to normal and atretic follicles, showed, on the one hand, the presence of a large corpus albicans which evidently represented the residue of the corpus luteum preceding the pregnancy. On the other hand there was no evidence of a recent corpus luteum, but there was found a large convoluted follicle with an edematous internal theca, and this was judged to date from the December cycle. The author therefore concludes that in the December cycle there had been a perfectly normal ovulation but that the lutein transformation of the ruptured follicle had not taken place. This leads the author to the generalization that so-called anovulatory cycles as a rule behave in the same manner as do the ovulatory; that is to say, ovulation occurs, but for lack of the production of the corpus luteum in the dehiscent follicle these cycles are "aprogestative." The results are the same, as the ovum cannot find the necessary conditions for fixation and development. The cycle thus consists of a single prolonged folliculin phase rather than two. The author does not, however, deny the possibility that anovulatory cycles can occur in the human female.

## THE MENSTRUAL CYCLE

### BASAL BODY TEMPERATURE GRAPHS AS AN INDEX TO OVULATION

PENDLETON TOMPKINS

J. Obst. & Gynaec. Brit. Emp., 52: 241-52, June, 1945

It now appears that the basal body temperature of woman is directly related to the phases of the menstrual cycle. The author purposes, in this report, to illustrate temperature curves in non-pregnant and pregnant women and to suggest that temperature graphs may constitute a valuable instrument of investigation, especially in the study of infertility.

Some 60 private patients kept the temperature graphs, recording their daily temperatures, menstrual periods and dates when intercourse occurred. In order to assure uniformity, temperatures were taken per rectum before arising in the morning or taking any foods or liquids. The high intelligence of the group and the fact that most of the patients were eager to conceive assured excellent co-operation.

The resulting graphs show that the temperature is relatively low prior to ovulation, shifts to a higher level about the time of ovulation, and maintains this higher level until the next menses when it falls and the cycle is repeated. In most cases, regardless of the length of the cycle, the temperature shift occurs approximately 14 days before menstruation.

From a study of the graphs, basal body temperature records may be put to the following uses:

1. As an index of ovulation to determine the time of maximal fertility for those who wish to conceive and to determine the "unsafe" period for those not using contraceptives.
  2. As a suggestive sign of early pregnancy ("The poor man's Friedman test").
  3. As an aid in evaluating treatment intended to stimulate ovulation.
  4. As an aid in securing biopsies in the preovulatory (proliferative) or post-ovulatory (secretory) phases of the endometrium.
  5. As an aid in the search for early human ova, unfertilized, fertilized or nidated.
  6. As a method of establishing a measure of "control" in studying the effectiveness of contraceptives.
  7. As a means of investigating some types of irregular uterine bleeding.
- 4 references.

(That the basal body temperature of women is directly related to the phases of the menstrual cycle will be conceded by everyone, but there is still considerable difference of opinion as to the practical value of this fact. Some are very enthusiastic about the method; others have not warmed up to it at all. Although seven advantages of the procedure are enumerated by the author, the fact remains that its chief indication has been in the management of sterility. I know of no evidence adduced by this plan of study which conflicts with the

accepted viewpoint as to the ovulation span. The author himself states, for example, that regardless of the length of the cycle, the temperature shift occurs approximately 14 days before menstruation, as Ogino and others have urged for many years.

Granted that the exact date can be determined by the careful application of the basal temperature method, one must decide for himself if this extra information offers sufficient advantage over the simple plan of advising that coitus take place frequently during the comparatively short span of the optimum period. It must be remembered, in making such a decision, that the ovum is believed to retain its fertilizability for a good many hours, perhaps as much as 24, and that the spermatozoan is believed to maintain its fertilizing potency for at least 30 hours. It should also be remembered that the method is far more valuable in the intelligent type of patient, such as those reported by Tompkins, than in those of less intelligent type, and that definite possibilities of errors in interpretation exist, as Tompkins and others have emphasized.

It is still too early to predict whether the method will gradually achieve wide adoption, or whether it will gradually die a natural death, and this is said in no disparaging way. Perhaps a good compromise plan would be to recommend this diagnostic aid in those women whose intelligent cooperation can be assumed, while for others the customary advice as to the optimum time for fertilization might be considered to suffice.—Ed.)

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(The idea which Dubreuil appears to convey is that many of our supposed anovulatory cycles are really cases in which ovulation actually occurs, but in which luteinization fails. The evidence which he presents for this is very incomplete, although he is correct in saying that the physiologic results would be the same in either case. The prevailing viewpoint, and this has far more support than Dubreuil's concept, especially from the study of anovulatory cycles in monkeys, is that ovulation fails to occur, the follicle simply ceasing its functional activity and degenerating at or perhaps shortly after the usual time of ovulation.—Ed.)

## DIETHYLSTILBESTROL IN THE TREATMENT OF FUNCTIONAL OVARIAN DISORDERS

CAPTAIN GEORGE D. PATTON, M.C., U.S.A.

Am. J. Obst. & Gynec., 50: 417-21, October, 1945

The author gave diethylstilbestrol in 5 mg. doses, for twenty days, to any patient who had one of the so-called functional ovarian disturbances, including dysmenorrhea, simple cystic ovaries, irregularity in menstrual rhythm, menorrhagia and infertility. The drug was administered to 107 women with 232 functional ovarian complaints. Approximately one-half of the patients had nausea of varying degree, and 9.3 per cent stopped taking the drug because of the severity of this symptom. Usually the nausea ceased if the patient persisted with the treatment. Nervousness was often relieved during the course of treatment. Uterine bleeding during the therapy was unpredictable, sometimes being normal as to time and duration, and sometimes abnormal. Because this was upsetting to the patients' peace of mind, it was decided to start therapy at the end of a menstrual flow. Withdrawal bleeding occurred within eight days in all cases except two, and the next menstrual flow occurred 28 to 35 days later and was designated as the first normal menses, the first bleeding to occur as the result of the cyclical activity of the ovary.

Partial or total relief was obtained in 56 per cent of the patients with dysmenorrhea. Ovaries returned to normal size in 37 of 47 patients with cystic ovaries. In 13 of 14 patients continuous uterine bleeding ceased after one to four days. Of all menstrual disturbances 70 per cent were partially or entirely corrected.

Due to the fact that the patients seen were in the Army clinics and the tenure of these patients temporary, the infertility study is not complete; however, 26 per cent conceived.

It was suggested that all the disorders considered are but different manifestations of a malfunctioning ovary. From the clinical standpoint, diethylstilbestrol, in the dosage used, corrected the symptoms of ovarian dysfunction in the majority of cases.

Four tables. Five references.

(This paper apparently advocates a charming simplification of the whole mixed-up problem of gynecological organotherapy, since diethylstilbestrol alone apparently answers

all purposes in pretty nearly all indications. I am inclined to agree with the author that if only one drug were available, diethylstilbestrol would probably more often be helpful than any other. I am sure he would not wish to undertake to give the rationale for the use of diethylstilbestrol in all the indications he has enumerated, and he will probably agree that in some cases more harm than good would be done. To give but one example, such doses as he recommends would certainly lessen fertility in some cases by inhibiting ovulation, as can be readily done by diethylstilbestrol begun postmenstrually, as he advises. None of us can brag about our results in gynecological organotherapy, and most of us are guilty of occasional slips into empiricism, but we should at least try to be as discriminating as possible in our use of endocrine preparations. While it is true that these various disorders are "different manifestations of a malfunctioning ovary," the mechanisms of these malfunctions show wide variations. It would seem unfortunate if the gynecologist had to limit himself to one arrow for his organotherapeutic bow.—Ed.)

## THE TREATMENT OF PRIMARY DYSMENORRHEA WITH DEPROTEINATED PANCREATIC EXTRACT (DEPROPANEX)

LAWRENCE L. GROSSMANN

Am. J. Obst. & Gynec., 50: 411-16, October, 1945

This article deals with a new treatment for primary dysmenorrhea. There have been many theories advanced for the cause of primary dysmenorrhea and any number of methods of treatment developed, with no great success; even surgical intervention has not proven satisfactory. Recent investigation has indicated that dysmenorrhea occurs only in the presence of active uterine contractions and that these are spastic in character.

In the past few years a number of endocrine substances have been used in attempts to relieve dysmenorrhea, but with little effect. Search was made for a preparation which was non-toxic and would produce the desired effect rapidly and with reasonable certainty, by diminishing the contractions of the menstruating uterus. A review of the literature revealed that a suitable preparation was available, but had been employed almost exclusively in peripheral vascular disease and in urology,—this was depropanex. Depropanex is a saline solution of a chemically derived, protein-free nitrogenous fraction obtained from acid-alcohol treatment of beef pancreas. It is free of insulin, histamine and acetylcholine. The dose recommended in the current literature is from 2 to 5 cc., given intramuscularly.

The series of cases studied by the author consisted of workers in two industrial plants and a group of private patients. There were 31 of the former and 25 of the latter. In the industrial series the treatments were given by the nurses at the plants, and since there was little or no information in regard to the dosage in the treatment of the condition, it was thought advisable to begin with less than the minimal dose of depropanex recommended for serious circulatory and urologic disorders. Orders were given for 1.5 cc. of the drug to be administered

intramuscularly, and this appeared sufficient in most cases, but in some instances was increased up to 4 cc. This regimen was also carried out for the private patients, the 25 women in this group receiving 63 treatments of from 1.5 cc. to 4 cc. Complete relief from dysmenorrhea was afforded within from fifteen minutes to one hour subsequent to the administration of fifty treatments (79.4 per cent). Partial relief was afforded within the same period of time after eleven treatments (17.5 per cent). Complete or partial relief, therefore, was obtained in the 25 patients on 61 occasions representing 96.9 per cent of treatments administered to the group. The 31 patients in the industrial group received 41 treatments, 22, or 53.7 per cent of which afforded complete relief, and 6, or 14.6 per cent, afforded partial relief from dysmenorrhea. Favorable response was denied after 13 treatments (31.7 per cent).

The striking disparity between the two groups is due to several factors. In the industrial group the labor turn-over made it frequently impossible to follow up the patients or repeat the medication. Some employees resisted parenteral treatment, and often denied any beneficial effects after the extract was administered. In most cases the denial was not borne out by the clinical appearance of the patient. The experience among the private cases was different, and definite, uniformly successful results were obtained in nearly all instances, the degree of relief varying somewhat in individuals, but in no case did the patient state no relief whatever was obtained from the extract. A noticeable decrease in pain occurred in most patients within 15 minutes after the drug was given and sometimes the pain had almost disappeared by that time. In other individuals relief was more gradual and from 30 minutes to one hour was required for the amelioration or disappearance of symptoms. A few patients noted that after several treatments the symptoms diminished to such an extent that further treatment was unnecessary.

The case history of one patient is given; a twenty year old woman, who had had severe dysmenorrhea since the menarche at 14 years of age, having been incapacitated from one to three days throughout her menstrual life. She was unmarried. Thorough study had failed to elicit any cause for such severe dysmenorrhea.\* Depropanex was administered on two occasions, in amounts of 2 and 4 cc. respectively, with no favorable results. A presacral neurectomy was performed during the ensuing month. The following menstrual period was extremely painful. After pain had continued four hours with no abatement, 2 cc. of depropanex were administered intramuscularly. Partial relief was obtained in fifteen minutes and almost complete disappearance of pain in one hour. On three subsequent occasions the same experience was observed. The symptoms are now gradually decreasing in severity and during the last menstrual period no medication was necessary; moreover, the patient has not been totally incapacitated as formerly.

The results of the investigation indicate that deproteinized pancreatic extract is very effective in the treatment of dysmenorrhea and that the favorable response is probably due to the spasmolytic action of the depropanex on the uterine muscle. It would seem from the results of the study, that depropanex is a most

valuable agent for the relief of dysmenorrhea and merits the attention of the profession for more extensive clinical evaluation. 1 table. 24 references.

(It is to be hoped that there will be no general rush to treat patients with "deproteinized pancreatic extract" until there is further evidence that it has some value. The countless remedies, chiefly supposed antispasmodics or inhibitors of uterine contractility, which have been suggested in the past and which have sooner or later passed into the discard, are reason enough for such skepticism. There is much plausibility in the prevalent view that exaggerated contractility of the uterine muscle is responsible for the pain of primary dysmenorrhea, but this viewpoint has certainly not been established beyond doubt. There is still much difference of opinion, too, on the roles of estrogen and progesterone in this respect, especially of the latter. Most important, it remains to be shown that "deproteinized pancreatic extract" is really an inhibitor of uterine contractility. Because of the subjective nature of the disorder and the frequently associated psychogenic factor, one must be doubly cautious in evaluating the results of treatment of primary dysmenorrhea.—Ed.)

## VULVA AND VAGINA

### ADHESIONS OF THE LABIA MINORA IN CHILDREN. A REVIEW OF THE LITERATURE

ROBERT E. JENNINGS

Urol. & Cutan. Rev., 49: 529-531, 1945

This review of the literature on adhesions of the labia minora from 1927 to 1944 is concerned with the symptoms, etiology, differentiation of this condition from vaginal atresia and pseudohermaphroditism, and correction of the condition. It is concluded that fusion of the labia minora is an acquired defect, and, although originally described as a condition of young children, several cases have been reported in which labial fusion either persisted into adulthood or began in elderly women, particularly unmarried women leading a sedentary life. Fusion of the labia minora is generally due to the formation of adhesions between the labia minora, forming a partial diaphragm distal to the urethral and vaginal outlets. At first these adhesions are thin and friable, but may become more densely organized as the condition persists. Among small infants there are no outward indications that the condition exists and no symptoms, as the outflow of urine is not impeded. In older infants, and in children aged three to eight years, the presenting symptom is dribbling or dysuria due to backing up of the urine into the vagina. Except in very long-standing cases, correction of the condition can be readily accomplished by blunt dissection of the fused labia minora without anesthesia.

(As the author states, it is remarkable how closely this comparatively simple condition can simulate and be mistaken for more serious ones, especially pseudohermaphroditism. There would seem to be no doubt that the common cause is simple inflammatory adhesion of the labia minora. In fact, in all of those which I have personally seen, the condition was readily correctible by gently, or rather forcibly if the adhesions are firmer, pulling the adherent labia apart. I have seen no cases in which the condition persisted into later years, when the adhesions might well have become so firm that simple plastic procedures might be necessary for correction.—Ed.)

### MALFORMATIONS VULVAIRES CHEZ DEUX FILLES NOUVEAU-NÉES

RAVINA AND JAMAIN

Gynec. et Obst., 44: 20, 1944-45

In the first case reported here the infant presented a lesion of the posterior part of the hymen. A small, V-shaped mucous growth, 1 cm. long, protruded from the vulva but it could be observed that it belonged to the hymen. No secretions nor vaginal discharges were observed.

In the second case the infant presented at birth an inflammation of the vulvar region. The labia majora were congested and red. A hymenal corolla issued from the vulva and a tapering appendage extended about 2 cm. below the level of the posterior part of the hymen. The vulva was separated from the anus by only a few millimeters, but both orifices were distinct. There were no anal malformations and the thickness of the vagina was normal. Examination of fluid withdrawn at the level of the vulva showed numerous vaginal cells. Culture on agar showed the presence of colibacilli, staphylococci and Gram-positive bacilli. Ablation of the growth was a simple procedure, without hemorrhage or perforation of the rest of the hymen. On section of the growth a mass of connective tissue and a number of vascular cavities were revealed. Most of the vessels were small. A diagnosis of angioma was ruled out by the authors. It seemed more to resemble a cicatricial sequel of an inflammation or a traumatic lesion.

### THE TREATMENT OF TRICHOMONAS VAGINITIS WITH A SULFONAMIDE COMPOUND

HELEN M. ANGELUCCI

Am. J. Obst. & Gynec., 60: 336-38, September, 1945

The author describes the treatment of one hundred cases of *Trichomonas vaginalis* infestation in nonpregnant women with a lactose-allantoin-sulfanilamide compound.

The pathogenicity of the organism, *Trichomonas vaginalis*, is yet definitely to be proved. It can be said also that there is no specific therapeutic agent. The extreme variability in the reaction of different patients to the same treatment caused the author to feel it necessary to search for the method of therapy which, while at least giving as good results as any other method, does so with the least inconvenience and discomfort to the patient.

The medication used in this study consists of an ointment containing 15 per cent sulfanilamide, 2 per cent allantoin, and 5 per cent lactose in a greaseless base, buffered to pH of 4.5 with lactic acid. It is expressed into the vagina by an applicator, delivering about 10 Gm. per dose, twice a day. It is odorless, nonstaining, nonirritating, appears to spread over the vaginal and vulvar surfaces, and is free from messiness, not necessitating pad or tampon.

One hundred patients were seen for periods of from four to ninety-one weeks. The average period of actual treatment was eleven weeks. Good results were considered to be: subsidence of symptoms, disappearance of trichomonads, and return of the vaginal mucous membrane to normal. A cure was a period of six months without treatment, with freedom from symptoms and recurrences. A failure was a case in which the trichomonads did not disappear during the course of treatment, four weeks being considered a reasonable period of trial.

Good results were obtained in 98 per cent of cases, permanent cures in 84.6 per cent, and failure in 2 per cent. The method was found therapeutically satisfactory and esthetically acceptable to the patient. 3 references.

## THE UTERUS

### THE VAGINAL SMEAR IN DIAGNOSIS OF CARCINOMA OF THE UTERUS

OLIVE GATES AND WARREN SHIELDS

Am. J. Pathol., 21: 567-601, 1945

This study is based on 341 vaginal smears from 233 patients, mainly from the out-patient gynecologic clinic of the New England Deaconess Hospital, Boston. The authors were primarily interested in the practical aspects of the vaginal smear as a procedure for the routine diagnosis of the presence or absence of uterine carcinoma, what can be expected of the method, and the pitfalls in diagnosis. The stain developed by Papanicolaou was used in nearly all of the smears; the others were stained with hematoxylin and eosin, a method which was found satisfactory. The interpretation of each smear, based on pathologic criteria, is given, and then correlated with other data pertaining to the particular case.

Nuclear changes were found to be the most reliable criteria of malignancy. These nuclear changes are variable, but a nucleus larger than normal in relation to its cytoplasm, or a relatively large one with unusual appearance or arrangement of chromatin, should arouse suspicion. The nuclei of malignant cells may be pale and finely powdered with granules; occasionally the chromatin is coarse, and scattered and sometimes closely attached to the nuclear membrane. In some malignant cells the nucleus was granular and took a homogeneous deep basophilic stain, but these cells usually showed some evidence of degeneration. The significance of mitotic figures in smears is negligible; such figures were seldom seen, and appeared also in smears in which the cells were atypical but not clearly malignant. Striking variation in size of cells was also found not to be of significant diagnostic value, as nonmalignant normal and pathological cells are variable in this respect. However, confirmation was made of Papanicolaou's statement that within a group of cells anisocytosis is quite significant. The arrangement of carcinoma cells in clumps of three or four was not conspicuous in the authors' series. Sheets of cells were seen most often in cervicitis, vaginitis, and radiation reaction.

As single malignant cells do not always carry distinctive features indicating their origin, and those seen in patches often bear little resemblance to the normal cell types of the uterus seen in section, the classification of the type of carcinoma on the basis of the smears is more difficult than the recognition of malignant cells. However, in differentiating carcinoma of the endometrium, the presence of endometrial cells in the smear, except during menstruation, is abnormal, and an unusual number or clumping of endometrial cells is strong evidence of adenocarcinoma. Many of the cells are vacuolated with eccentric nuclei of signet ring type. In undifferentiated carcinoma the cells may be very small, with dark basophilic nuclei and only fine tails of cytoplasm.

In the authors' total series, the smears from 101 patients were classified as nonmalignant and 132 as malignant. In all but four of those classified as malignant there were positive biopsies, and clinically those four were unquestionably carcinoma. Only 33 of the malignant cases were not radiated. The cases classified as nonmalignant were considered clinically benign; biopsy had been performed on only 36.

The smears taken during or after radiation treatment were more difficult to analyze. Frequently they were unsatisfactory because of degeneration, but the greatest difficulty arose from an uncertainty of interpretation of the cases in which radiation reaction was present. Two prominent features of smears showing radiation reaction are: (a) a high proportion of "basal" cells, and (b) variation in their appearance. These "basal" cells are large with swollen nuclei, which tend to be pale rather than hyperchromic or very small with deeply pyknotic nuclei. They usually vary in shape as well as in size. Heavily spotted nuclei, with large distinct clumps of chromatin, sometimes without a nuclear membrane, may be seen in cervicitis and are identical with nuclei in some early epidermoid carcinomas or in a grade I epidermoid carcinoma. Some of these atypical cells were seen in patients who had remained without evidence of disease five or more years after radiation treatment. Some of the cell changes prominent in radiation reaction were also seen in nonirradiated elderly patients, and were usually associated with infection. In radiation reaction, however, there were more cells that differed from one another in appearance and usually more anaplastic cells than were seen in nonradiated benign conditions. The extent of radiation reaction was unpredictable in that it does not seem to be correlated with either the time element or the amount of radiation.

In the authors' series, 46 of 157 smears showed definite radiation reactions, and 23 were suggestive of such reaction. On the other hand, there were 10 smears which seemed to show radiation reaction, but the patients had not been irradiated.

There were four cases in which a positive diagnosis on the smear was the first evidence of carcinoma: a case of carcinoma in situ; three cases of "hidden" or unsuspected carcinoma, including an adenocarcinoma and one postradiation recurrence.

Tables are presented showing first diagnoses and final diagnoses (i.e., rereadings after experience in analysis) from the smears, and clinical and biopsy diagnoses for each case.

It is concluded that: (a) untreated carcinoma of the cervix of low to moderate malignancy may be easily recognized from the smear, but carcinoma of the cervix of high malignancy, sloughing tumors, adenocarcinomas of the endometrium and endocervix, as well as the irradiated carcinomas, may be recognized only with difficulty even by pathologists familiar with the method; (b) the smear may be of value as a screening test for detecting the existence of cervical or endometrial cancer in large groups of women; (c) it may be valuable in diagnosis to detect recurrence after radiation since in these cases biopsy is preferably avoided; and (d) it may be useful as a subsidiary test in cases of "hidden carcinoma."

## THE UTERUS

### THE VAGINAL SMEAR IN DIAGNOSIS OF CARCINOMA OF THE UTERUS

OLIVE GATES AND WARREN SHIELDS

Am. J. Pathol., 21: 567-601, 1945

This study is based on 341 vaginal smears from 233 patients, mainly from the out-patient gynecologic clinic of the New England Deaconess Hospital, Boston. The authors were primarily interested in the practical aspects of the vaginal smear as a procedure for the routine diagnosis of the presence or absence of uterine carcinoma, what can be expected of the method, and the pitfalls in diagnosis. The stain developed by Papanicolaou was used in nearly all of the smears; the others were stained with hematoxylin and eosin, a method which was found satisfactory. The interpretation of each smear, based on pathologic criteria, is given, and then correlated with other data pertaining to the particular case.

Nuclear changes were found to be the most reliable criteria of malignancy. These nuclear changes are variable, but a nucleus larger than normal in relation to its cytoplasm, or a relatively large one with unusual appearance or arrangement of chromatin, should arouse suspicion. The nuclei of malignant cells may be pale and finely powdered with granules; occasionally the chromatin is coarse, and scattered and sometimes closely attached to the nuclear membrane. In some malignant cells the nucleus was granular and took a homogeneous deep basophilic stain, but these cells usually showed some evidence of degeneration. The significance of mitotic figures in smears is negligible; such figures were seldom seen, and appeared also in smears in which the cells were atypical but not clearly malignant. Striking variation in size of cells was also found not to be of significant diagnostic value, as nonmalignant normal and pathological cells are variable in this respect. However, confirmation was made of Papanicolaou's statement that within a group of cells anisocytosis is quite significant. The arrangement of carcinoma cells in clumps of three or four was not conspicuous in the authors' series. Sheets of cells were seen most often in cervicitis, vaginitis, and radiation reaction.

As single malignant cells do not always carry distinctive features indicating their origin, and those seen in patches often bear little resemblance to the normal cell types of the uterus seen in section, the classification of the type of carcinoma on the basis of the smears is more difficult than the recognition of malignant cells. However, in differentiating carcinoma of the endometrium, the presence of endometrial cells in the smear, except during menstruation, is abnormal, and an unusual number or clumping of endometrial cells is strong evidence of adenocarcinoma. Many of the cells are vacuolated with eccentric nuclei of signet ring type. In undifferentiated carcinoma the cells may be very small, with dark basophilic nuclei and only fine tails of cytoplasm.

experimental knowledge that once an experimental malignant state has developed as the result of an oncogenic stimulus the malignancy may continue in the absence of the original initiating mechanism. In other words a cancer cell probably remains a permanently altered cell.

Theories, past and present, on the origin and etiology of cancer and work on the experimental production of cancer in animals by the use of chemicals and estrogenic substances are discussed briefly. Up to the present time experimental cancer has not been produced in the monkey or any rodent other than the mouse. The author brings out this fact in order to reveal the tenuous structure on which some base their fear of inciting human cancer from the use of estrogens. Before one applies the highly artificial results on rodents unreservedly to the human being it is important to consider that various species of rodents may vary in their response to substances other than tumor initiators and that this field of experimentation is fraught with pitfalls, not only for the inexperienced investigator but also for the clinician who attempts to find an immediate clinical application. However, this does not imply that no relationship may be shown later to exist between endocrine stimuli and human neoplasia.

At the present time it is not known definitely whether cancer begins from a focus of a single cell or a group of cells, whether it originates by transformation of a preformed normal cell, whether a previously normal cell gives spontaneous origin to cancer cells abruptly during the process of cell division, or whether this change occurs gradually through a series of cell division. One cannot say from histologic appearance whether a given cell or group of cells showing a non-invasive carcinomatoid change are destined to maintain their present status, regress to normal or go on to obvious malignant change. Because of this the question of so-called non-invasive carcinomatoid lesions in the cervix uteri is still nebulous and unsettled.

Martzfloß expresses the opinion that an impasse in the solution of these problems has been reached, that much of the investigation being done now is a form of repetition, and that it is probable that new techniques and basic discoveries in allied sciences will have to occur before the underlying mechanism of tumor production is solved.

The treatment of cancer of the cervix is considered as having progressed through two distinct eras: first, the exclusively surgical era, and, second, the present radiological era. From the standpoint of surgical treatment, the present century may be said to have offered a more rational attitude toward some of the fundamental principles first evolved. In the light of greater experience and study it has become understandable why fulfillment of some of the theoretical aims of the radical operation were often not attainable in practice. The three primary anatomical zones to which cancer of the cervix tends to produce comparatively early extension or metastases are the ones which the radical operation in its fundamental concept aimed to remove. However, under conditions of actual trial, radical surgery alone has proven itself generally incapable of success when extrauterine extension of disease other than to the vagina has occurred. The limitations of effective procedure have now been delineated, although the

(Since the publication of the monograph by Papanicolaou and Traut in 1943 (Papanicolaou, G. N., and Traut, H. F., *Diagnosis of Uterine Cancer by Vaginal Smear*. New York: Commonwealth Fund, 1943) only a few studies have been reported by others. The most important of these are those of Meigs and his coworkers, and that of Gates and Shields, abstracted above. The two papers by Meigs and his group, the second of which appeared very recently (Meigs, J. V., Graham, R., Fremont-Smith, M., Janzen, L. T., and Nelson, C. B. *The Value of the Vaginal Smear in the Diagnosis of Uterine Cancer*. *Surg. Gyn. & Obst.* 81: 337, 1945) was based on the study of 1015 patients, and the conclusions of the authors were perhaps more enthusiastic than those of Gates and Shields, although they also pointed out certain limitations of the method.

There would seem to be no doubt that even in early stages of cancer there is some degree of desquamation of cancer cells from the lesion. One's first thought would be that the diagnosis of cancer in the highly attenuated form represented by the vaginal smear could scarcely be as decisive as the diagnosis made by biopsy or curettage from the concentration of cancer cells represented by the lesion itself, and this view is probably correct. It is probable, too, that most gynecological pathologists will feel that not a great many cancers are missed by properly performed biopsy or curettage, though occasional exceptions may occur, and repetition of the procedure may be called for in the occasional early case. Again, when biopsy is improperly done, or when it misses the site of very early lesions, or when microscopic study is not sufficiently thorough, the percentage of mistakes is obviously increased.

On the other hand, diagnosis by vaginal smear clearly presupposes an expert knowledge of cytology, for it often means a diagnosis based on the morphology of single cells. It is quite certain that it will not replace biopsy as a decisive diagnostic method. Both Gates and Shields, as well as Meigs and his group, suggest that the chief value of the method may be as a screening test in the detection of cancer in larger groups of women, and it is entirely possible that it might therefore prove of great value in the campaign against cancer. One can not recommend routine or periodic biopsy or curettage in ostensibly normal women, but it should not be difficult to persuade such women to submit to periodic vaginal smears. If such smears were examined by expert cytologists, working perhaps in state departments of health, it is possible that a good many unsuspected cases of cancer might be brought to light.

It is to be hoped that the method will be further investigated in well organized clinics. It would seem to be a good plan to train one or more members of gynecological staffs intensively in this field, for in no other way can one acquire the cytological acumen necessary to employ the method intelligently or profitably. There will no doubt be further reports on results from time to time, and we shall probably have frequent opportunity in the future for further evaluation of the method.—Ed.)

## CANCER OF THE CERVIX UTERI. SOME FUNDAMENTAL CONSIDERATIONS

KARL H. MARTZLOFF

*West. J. Surg., Obst. & Gynec.*, 53: 255-267, 1945

This paper begins with a brief review of the history of the recognition of the pathology of cancer in general and cancer of the cervix in particular. The fundamental pathologic anatomy of cancer of the cervix was thoroughly recognized and described in the nineteenth century. The present century has only contributed a better clinical and pathologic correlation of the disease and the

## FACTS AND FIGURES ON CANCER OF THE CERVIX AND ENDOMETRIUM AND THE INCIDENCE OF THESE DISEASES IN A METROPOLITAN CITY OF TEXAS

T. R. HANNON

Texas State J. Med., 41: 186-190, 1945

During the year 1944 there were 192 patients with cancer of the cervix and 37 with cancer of the fundus admitted for treatment in five of the larger hospitals of Houston, Texas. This represented an incidence rate of 48.2 cases per 100,000 population, a figure slightly lower than the 53.5 cases per 100,000 population quoted by the United States Public Health Service for the total urban population of the country. The highest percentage (25.5) of the women with cervical cancer was in the 40-to-50-year age group; 72.9 per cent were between 30 and 60 years of age. The lowest percentage (4.2) was between 20 and 30 years of age. Similarly, the majority of those with cancer of the endometrium were over 30 years of age, the percentage distribution for each decade being approximately equal.

An analysis of the presenting symptoms demonstrated that the majority of the patients were admitted with symptoms indicating that the disease was already far advanced, and at the time of hospital admission showed evidence of metastasis and obstruction, cachexia and pressure. The largest percentages of cases were in Stages III and IV.

A great variation in methods of treatment was found. Surgery ranged from total hysterectomies (some with one or both ovaries left unremoved) to vaginal hysterectomies without the removal of adnexal organs. The type and dosage of radium therapy also varied considerably, and frequently appeared inadequate on the basis of recognized present-day therapy dosage. The type and dosage of x-ray irradiation could not be determined from a review of the hospital records.

No data are presented on the outcomes following treatment or mortality rates in the series. It is, however, pointed out that the survey emphasizes the need for physicians who are better trained and more diligent in the early diagnosis of these diseases, and better acquainted with the recognized standard methods of treatment.

In the discussion of this paper, Allen L. McMurray, of Houston, states that he has cured, with no evidence of recurrence, cases of carcinoma of the cervix by superficial conization for biopsy. Several of his patients were in the twenties and early thirties. Karl J. Karnaky, also of Houston, expressed the opinion that the majority of 709 cases of cancer treated at the Jefferson Davis Hospital could have been prevented by cauterization or coagulation of the cervix. Among over 5,000 women on whom conizations had been done not one developed a carcinoma of the cervix.

(It would be fine if an analysis of this sort could be made in other communities; if, for example, every death from pelvic cancer were subjected to impartial review to determine whether the patient had had the benefit of early diagnosis and adequate therapy, and if not,

more or less isolated experiences of Bonney and a few others must be considered. The essential correctness of this is corroborated by the fact that the percentage of so-called five-year cures obtained by the vaginal operation is about the same as for the abdominal procedure, i.e., varying from 30 to 50 per cent.

At the present time it is probable that the increased success of radiation therapy is due to its greater effectiveness in destroying cancer in the cervix proper and its immediate peripheral zone rather than to any markedly effective action on cancer infected lymph nodes. An occasional opportunity to observe superficially situated metastatically involved lymph nodes which receive competent maximum deep roentgen ray therapy only to find them harboring viable cancer cells months later when they are removed, serves to confirm this impression. As far as one can now ascertain, there probably is no acceptable proof available that radiation therapy as now employed for cancer of the cervix destroys metastases in the regional lymph nodes with any degree of regularity.

It is also recognized that a cancerous cervix which has healed after radiation and assumed an essentially normal appearance may still harbor histologically demonstrable viable cancer in from 20 to 30 per cent of patients so treated. This has been observed within a few millimeters of the cervical canal where a total of 3,000 mgh. had been previously directly applied.

For the present it seems that as a minimum the field of radiation therapy in cancer of the cervix uteri should comprise: (1) its preoperative use in ulcerative carcinoma that is to be subjected to operation; and (2) its use in operable cancers in women who are obvious poor operative risks. The spindle cell group of epidermoid cancers which have been shown to possess such a poor prospect of salvage by operation alone, and such a high degree of curability by radiation both in early and advanced disease offer a special problem for the combined treatment.

It is pointed out that the high mortalities once experienced by surgery for cervical cancer were due largely to operative shock peritonitis or postoperative nonembolic pneumonia. Due to better anesthesia as well as preoperative and postoperative care, shock is now a minor factor in proper surgical risks. Postoperative peritonitis has also decreased since preoperative radiation is being used. It is concluded that in order to obtain the best results from treatment with our present methods and with our present limited knowledge concerning this disease both radiology and surgery properly utilized offer a better outlook than one method singly employed.

(The author, whose studies and contributions in the field of cervical cancer are well known, presents a comprehensive and well-tempered review of the whole problem, and the conclusions he draws will meet with the approval of most gynecologists. His views on the possible hazard of estrogens in inciting cancer growth, emphasizing the fallacy of applying animal experiments indiscriminately to the human and calling attention to the absence of any evidence of carcinogenic hazard from ordinary therapeutic doses of estrogen, seem very sound, as does his discussion of the treatment of cervical cancer. Few will disagree with him as to the limited regional effect of radium therapy, and also its not infrequent local ineffectiveness, as shown by the finding of viable cancer cells in repeat biopsies. Nor will many disagree with him as to the extremely poor prognosis with any method of treatment once the disease has spread to the glands. The article presents very ably the present status of the whole problem.—Ed.)

entirely limited to the cervix. Group II. The carcinoma has infiltrated the parametrium on one or both sides; the upper two-thirds of the vagina or a portion of this area; if an inverting type of growth, the body of the uterus may be invaded. Group III. Infiltration has invaded the pelvic wall on one or both sides; on rectal examination there is no free space between the tumor mass and the pelvic wall. Frozen pelvis. All of the vagina involved. Group IV. The carcinoma involves the bladder or rectum. Fistulae may be present. It may have spread outside the true pelvis, above the pelvis, below the introitus; distant metastases may have occurred.

It is pointed out that vaginal bleeding may be a very late symptom of cervical cancer. The author has found some surprisingly early cases since he has made it a rule to biopsy every cervix which required treatment. This is a simple, rapid, inexpensive office procedure, which produces no harm and little discomfort to the normal patient.

In planning treatment and making prognosis other factors in addition to clinical and cell classification of the carcinoma should be taken into consideration. These include age of patient, her general health, size and obesity, the presence and extension of pelvic inflammatory changes, adhesions of bowel to adjacent structures, and the resistance the patient may or may not have to the malignancy. In general, the following rules are recommended.

Radical panhystero-bilateral salpingo-oophorectomy, with removal of upper one-third of the vagina is the procedure of choice in the following cases which are relatively radioresistant: (a) cell classification Broder's I, Martzloff's I, or spindle cell in squamous cell carcinoma (early), and clinical classification Groups Ia, b or c; (b) cell classification Broder's II, or Martzloff's transitional, and clinical classification Groups Ia or b; (c) Broder's III or IV, or Martzloff's spindle or basal cell, and clinical Group Ia. Irradiation on the hypogastric, external iliac and presacral lymph nodes may be employed, if necessary, following the operation.

A combination of x-ray, radium and operative procedures is recommended for cases in clinical Groups Ib and c, and cell classifications as noted in (c) above. In all cases in which the cells have invaded the tissues beyond the cervix, that is, from Group II on, irradiation by x-ray and radium is the procedure of choice.

The necessity of careful follow up during the course of therapy is stressed. For example, the clearing up of inflammatory changes following some x-radiation may show that what was originally thought to have been an extensive growth may have been only an induration from inflammatory changes. The patient may thus be placed in a lower clinical group with the corresponding change in course of therapy.

In the presence of infection, it is better to use x-radiation prior to radium, unless one has one or two grams of radium, and can expose the tissue to heavy doses at short intervals and very short duration of time at each exposure, and is able to clear up the infection by local applications in the form of sulfonamide, antiseptics, or penicillin. Another indication for x-ray, prior to radium, is the effect of x-rays in sealing off some of the lymphatics and blood vessels, so that

to try to fix the responsibility for the dereliction, for educational rather than punitive purposes. The now large group of maternal mortality committees operating in many cities have done a splendid work of this sort on another problem.

It is of interest to note that Philadelphia, which I believe took the lead in the maternal mortality work, has again taken the initiative through the creation, as recently announced, of a Philadelphia Committee for the Study of Pelvic Cancer (*Amer. J. Obst. and Gyn.* 50: 592 (Nov.), 1945). The primary aim of this Committee is the detailed study of the "delay period" in every case of death from pelvic cancer, and it is probably a wise plan to commence the project in this restricted way, though there would seem to be no reason why the scope of the study should not later be broadened somewhat along the lines indicated above. The Philadelphia Obstetrical Society is to be congratulated for its enterprise in inaugurating this new educational project.

Hannon's review of the Houston cases again reveals the depressing fact that the majority of cases are found to be advanced and often hopeless when treatment is applied for. It also illustrates the great variation in methods of treatment, and the fact that in a certain proportion the method chosen could scarcely be considered adequate. It is noted that in some cases treated surgically, one or both ovaries were conserved, which is contrary to standard concepts, in spite of the relative rarity of ovarian metastases in cervical cancer. It is of interest, however, to note that a few excellent gynecologists are showing a tendency to leave one ovary where panhysterectomy is done for cervical carcinoma in the younger group of patients.

I do not think that any experienced gynecologist will doubt that very early unsuspected cancer has in some cases been cured by very simple conservative measures, such as cauterization, conization, trachelorrhaphy, tracheloplasty or cervical amputation. In the older surgical era in the treatment of cervical cancer, allusion was often made to the fact that Byrne of Brooklyn had obtained just about as good results with his high cautery amputation of the cervix as were achieved by those doing the extensive radical operations of those days.

There will of course be a difference of opinion as to Karnaky's statement that "the majority of 709 cases treated at the Jefferson Davis Hospital could have been prevented by cauterization or coagulation of the cervix." This brings up the question of the predisposing role of chronic irritative lesions of the cervix, on which point there is emerging a difference of opinion. The question is too big a one to embark on here but we shall quite surely have occasion to comment upon it from time to time in the future. See also comments on two succeeding abstracts.—Ed.)

## TREATMENT OF CARCINOMA OF THE CERVIX BASED UPON CLINICAL AND CELLULAR CLASSIFICATION

JOHN D. WEAVER

Texas State J. Med., 41: 191-195, 1945

In the author's opinion Martzloff's and Broder's cell classifications of cervical carcinoma are satisfactory, but the clinical classification, as clarified by the Radiological Sub-commission of the Cancer Commission of the League of Nations in 1938, places too much emphasis on the late and hopeless case and offers no classification or subdivision for the early cases. The following clinical classification is proposed: Group Ia. Microscopic lesions; some cases only surface changes, clinically not recognized; "precancerous" or "suspicious." Group Ib. Macroscopically recognizable, but only surface involved. Group Ic. Cancer

ment of epidermoid carcinoma of the cervix in all stages. However, the fact remains that at the present time 20 per cent of Stage I and at least 30 per cent of Stage II cases are not cured by even the most competent and skillful radiation therapy. The question arises whether these failures represent types of the disease essentially not suitable for radiation therapy (and, if so, whether these lesions could be controlled by radical hysterectomy provided they are recognized prior to treatment) or whether they are due to other reasons which are not evident in a statistical evaluation. In an attempt toward clarification of this problem the authors analyzed the 19 failures among the 79 patients with carcinoma of the cervix in operable Stages I and II treated by irradiation at the Swedish Hospital Tumor Institute between 1935 and 1943.

Of the 19 patients, three with controlled carcinoma died of complications secondary to an intestinal irradiation necrosis. Two of these, of slight build, were treated early in the series when the dangers of supervoltage x-ray therapy were not sufficiently understood, and received a depth dose through large fields which was sufficient to cause lethal intestinal damage.

There were four patients with pelvic complications. One died of pelvic peritonitis following immediate postpartum treatment for a Stage II carcinoma and associated pelvic cellulitis. It is believed that this patient could probably have been saved by a more judicious and delayed conduct of therapy. Another patient in this group developed pyometra following treatment and died of a pelvic abscess in spite of repeated drainage. It is believed that the treatment was as good as possible and that death was unavoidable in the other two cases in this group.

The authors believe that two patients could have been saved by a better distribution of the dose in space. In both cases the parametrial dose was insufficient. In two cases treatment was incomplete (one, insanity; the other, mental attitude). Pulmonary metastases occurred in one case, and extrapelvic complications (pelvic disease controlled) in three cases. Four patients, listed as unexplained failures, died of parametrial recurrence.

Although none of the failures in the present series was due to uncontrolled or recurring cancer in the cervix itself, failure due to this cause does occur in rare instances, and is probably explained by an unusual radioresistance of the tumor. In the authors' total series of 135 cases of all stages there was observed only one regrowth in the cervix and this occurred after four years' freedom from demonstrable disease in a Stage III carcinoma in a patient 70 years of age.

From this study and reviews of Lacassagne's, Taussig's and Meigs' observations and views, the authors come to the following conclusions.

Early Stage I carcinomas have an excellent chance of permanent cure by radium only with one week hospitalization and no subsequent morbidity due to the treatment itself. For this type of case a procedure of the magnitude of the Wertheim operation seems unnecessary.

It seems that radiation therapy can control pelvic disease beyond the cervix if it represents a diffuse direct invasion through the lymphatics of the broad ligament but not disease in the lymph nodes. Therefore, apparently extensive

instrumentation may not accelerate the metastases. Following the use of x-ray, there is a decrease in the size of the lesion. This is an important fact in more advanced cases, because it gives a smaller area to radiate with the radium which has an effective range of no more than 3.5 cm.

The amount of x-radiation or radium, their direction and placement are discussed briefly.

It is pointed out that with the present knowledge and materials to prevent and treat shock, and the use of sulfonamides and penicillin to treat infection, the radical operation may become a relatively safe procedure.

(The fact that the author urges the advisability of subdividing the Group I cases of the League of Nations Classification is of interest, emphasizing the increasing intensiveness of study of early cases of cervical carcinoma. If such a subdivision is adopted, some such grouping as the author suggests would seem quite rational. It is rather surprising, though perhaps not too unfortunate, that the author did not see fit to distinguish between the so-called "pre-invasive" and "invasive" early lesions, a question which has given rise to much study and some differences of opinion.

As the author says, vaginal bleeding may in some cases not occur until the lesion has reached a fairly advanced stage, so that even an intelligent, alert patient may at times be doomed before this symptom is noted. There can be no criticism of his practice of subjecting to biopsy every cervix requiring treatment, even though this is a more advanced rule than that in more general use, of invoking biopsy in every lesion which is in any way suspicious.

Nor can there be any important objection to the general rules of treatment laid down by the author, recognizing the fact that at the present moment the matter of treatment appears to have again become somewhat unjelled. The radiotherapeutic enthusiasts, if one can find room for enthusiasm in any form of therapy for cervical cancer, still hold their fort, in spite of those who follow radiotherapy in certain cases with radical panhysterectomy, and the small brave band who, like Meigs, have made the complete revolution, given up radiotherapy and gone back to a Wertheim or super-Wertheim operative plan in selected cases. Most of us are quite willing for the present to stand on the side-lines and watch this experiment. It is undoubtedly justifiable to hope that improvements in surgical technique, transfusion, and sulfa and penicillin therapy will yield a far lower mortality than could have been possible in the earlier surgical phase of cancer therapy. However, it still remains to be demonstrated that the yield of cures in cases where there is extensive gland involvement will be appreciably greater than it was a generation or so ago, when it appeared to be the universal observation that recovery is rare indeed when the disease has spread to the glands—and probably beyond those accessible to pelvic operation. It will be interesting to see the results of this surgical resurgence unfold over the years, and we shall try to keep our readers abreast of developments in this field. See also comment on preceding and following abstracts.—Ed.)

## IRRADIATION FAILURES IN EARLY CERVICAL CANCER. IMPROVED IRRADIATION OR RETURN TO SURGERY

FRANZ BUSCHKE AND SIMON F. CANTRIL

Am. J. Roentgenol., 54: 60-71, 1945

It is now generally accepted that statistically the results of adequate radiation therapy are superior to those of the radical Wertheim hysterectomy in the treat-

frank and profuse bleeding in 76 cases and contact bleeding, occasional spotting or vaginal discharge in 69 cases. Sixty-one of the 76 patients had associated pathologic conditions (fibroids, fundal sarcoma or carcinoma, ovarian tumors, etc.) which could explain the bleeding more readily than could the cervical polyp. In the group of 69 with occasional spotting, chronic cervical infections and lacerations were observed frequently. The impression was gained that the infection and not the polyp was often the underlying cause for the spotting and blood-tinged discharge. In all, 33 per cent of the 228 patients were asymptomatic, and 80 per cent of the 99 patients without other pathologic conditions were free of complaints directly referable to the cervical polyp. Therefore, it is concluded that when a patient presents herself with the complaint of frank bleeding and a polyp is found on examination, care should be taken to exclude other causes of bleeding.

Uterine polyps were also encountered in women of all ages, but the largest number was found in patients between the ages of 41 and 50 years. A variety of associated pathologic conditions was found in 58 of the 82 cases.

The structures of both of these types of mucous polyps resemble those of the cervical and uterine mucosa, respectively, and generally show only slight variations. Secondary changes involving epithelium and stroma are frequent. The most important changes are nonmalignant epidermization in cervical polyps and malignancy in endometrial polyps. While a true polyp may become malignant, these changes are usually evident upon clinical examination and thus rarely cause confusion.

Although all of the cases in the present series were treated in hospital, it is felt that if the absence of serious associated pathology has been fully ascertained and if the symptoms of the patient can be explained by its presence alone, a simple cervical mucous polyp may be removed in the physician's office. The treatment of choice is excision and cauterization of the base.

(While this comprehensive statistical study has revealed no noteworthy new facts about cervical or endometrial polyps, it serves to emphasize some which are of clinical importance. For example, the authors very properly caution that the mere finding of a polyp in a patient who is bleeding should not lead one to assume that the polyp is the source of the abnormal bleeding, though it will often be found to be. The common practice of removing many cervical polyps in one's office is not in itself reprehensible if one bears in mind the possibility that other causes of bleeding, often much more important, may be present. There is no doubt, however, that a too casual attitude in this respect has not infrequently led to the overlooking of such lesions as early cervical carcinoma or submucous myoma, not to speak of bleeding of functional type.—Ed.)

disease of Stage III can be controlled in a certain percentage of cases while apparently less advanced stages in which the involvement of peripheral pelvic nodes cannot be demonstrated by palpation develop parametrial disease from these uncontrolled lymph nodes. Three of the four patients in the authors' series which belonged to this group would not have been accepted for surgery according to Meigs' standards. In Meigs' series of 65 patients on whom he operated nine belonged in this group, from which the authors conclude that three of 20 could be saved and 17 would be subjected to unnecessary surgery. Since it is impossible to recognize these cases prior to treatment, the authors consider it most likely that from a statistical point of view the actual survival rate by surgery would be smaller than if radical radiation therapy were instituted. They conclude that the survey of their own material has shown that more cases were not controlled by irradiation because of some avoidable inadequacies of treatment than would have been saved by surgery of cases essentially unsuitable for irradiation, and that improvement of radiation therapy by more careful attention to details of technique, by the elimination of inadequate procedures of the past and by the careful adaptation of the procedure to individual requirements will probably save more patients than a return to surgery.

(This paper is a good illustration of the widely differing attitudes of mind still revealed with reference to the most effective treatment of early cancer of the cervix. Only a few years ago we were all but universally ensconced in the almost exclusively radiotherapeutic approach, but now there seems to be a growing tendency toward combinations of radiotherapy and surgery, of one type or degree or another. The present authors have analyzed their 19 failures in 79 patients of Stages I and II, belonging presumably to the operable group, and conclude that even with due regard for the inadequacies of radiotherapy in this group, the results were better than could have been expected from surgery. It is remarkable that in only 1 of 135 cases of all grades was cervical regrowth observed. Excellent as are the usual local results of radiotherapy, post-radiation biopsies have in our experience shown a not infrequent persistence of what are obviously viable cancer cells. See also two preceding abstracts.—Ed.)

## POLYPS OF THE CERVIX AND UTERUS

KURT NEWGARD AND DANIEL G. MORTON

West. J. Surg., Obst. & Gynec., 53: 268-275, 1945

The authors made a review of the cases in which uterine polyps had been diagnosed at the University of California Hospital between 1930 and 1939. There were 228 cases with a diagnosis of cervical polyp and 82 with a diagnosis of endometrial polyp. This paper is concerned primarily with the former group. While cervical mucous polyps occurred in women of all ages, 60.9 per cent of the women in the present series were between 40 and 60 years of age; 23.7 per cent of the patients had never been pregnant. Only 99 (43.4 per cent) were without additional pathologic findings. Seventy-two had no gynecologic complaints whatsoever and the discovery of the polyp had been accidental. Among the patients with symptoms the most frequent complaint was bleeding. There was

OVARIAN NEOPLASMS. A COLLECTIVE REVIEW OF THE  
RECENT LITERATURE

MALCOLM B. DOCKERTY

Surg., Gynec. &amp; Obst., 81: Suppl., 179-204, 1945

The range of variety exhibited by neoplasms in the ovary is being continually expanded by the addition, from time to time, of what appear to be new oncologic entities. The discovery within this group of several members which exert a "physiological" influence on their host has led to exhaustive study of the hormone content of these neoplasms. Experimental production in animals of ovarian tumors has opened up a new field for investigating some fundamental histogenic problems. In the present review, the author attempts to evaluate current facts which have been established in these different fields of study and to correlate the data on the subject of ovarian neoplasms which have been published since July, 1938. More than 400 articles were consulted, and about 200 of these are listed in the bibliography. Endometriomas are omitted from the discussion because of their frequent occurrence as primary growths in locations other than ovarian, and because their origin has not been entirely agreed upon. Included in the review are: serous cystadenoma (serous cystoma, ovarian endosalpingioma, etc.); pseudomucinous cystadenoma (mucinous cystadenoma); carcinoma of the ovary; ovarian fibromas; dermoid cysts and complex teratomas; strumal tumors; granulosa-cell tumor; theca-cell tumor; arrhenoblastoma; adrenal-like ovarian tumor associated with Cushing's syndrome (so-called masculinovoblastoma, luteoma, hypernephroma, adrenocortical carcinoma of the ovary); dysgerminoma ovarii; Brenner tumor; mesonephroma of the ovary; and secondary tumors of the ovary including Krukenberg's tumor.

(This is an excellent and comprehensive review of a difficult subject, and it can be commended to the consideration of all who are interested in the study of ovarian tumors.—Ed.)

A CASE OF HEMOLYTIC ANEMIA RELIEVED BY REMOVAL  
OF AN OVARIAN TUMOR

EDGAR JONES AND CLIFFORD TILLMAN

J. Am. Med. Assoc., 128: 1225-7, 1945

For two years the patient had been complaining of a variety of symptoms, notably weakness, pain at various sites, mostly of the extremities, and a widespread, erythematous skin eruption. A diagnosis of dermatomyositis was made at two institutions. Subsequently, when seen at a third hospital, she had developed a marked anemia, the red blood cell count having fallen to 1.75

## THE ADNEXA

### THE SYNDROME OF OVARIAN TUMOUR ASSOCIATED WITH ASCITES AND PLEURAL EFFUSION (MEIGS' SYNDROME)

STUART R. TOWNSEND

Canad. Med. Assoc. J., 53: 245-247, 1945

This paper presents a case of multiovular cysts with ascites and pleural effusion in an unmarried woman aged 49. In 1940 she consulted her physician because of progressive swelling of the abdomen, weakness, and decrease of menstrual periods in amount and in lengthening of the interval between them. At examination a mass in the abdomen and a right pleural effusion were found, and a diagnosis was made of inoperable carcinoma, with metastases to the lung. Following this diagnosis, the patient endured severe suffering, remained bed-ridden and refused operation for two years. In May, 1942, the tumor had become the size of a nine-month pregnancy, was irregular in outline, slightly movable and gave the impression of being cystic. There was evidence of bilateral pleural effusion. There was no dependent edema. In June the patient accepted operation, and a total hysterectomy and bilateral salpingo-oophorectomy was performed. Recovery was uneventful and rapid and within three weeks after operation the pleural fluid had entirely disappeared. Three years later the patient was still alive and well, with excellent nutrition and a gain in weight of from 78 to 140 pounds. Microscopic examination of sections of both ovaries showed papillary cystadenocarcinoma. Sections of the abdominal wall and peritoneum revealed marked thickening and fibrosis with chronic inflammatory cells. There was no infiltration.

To the present time 27 cases of benign tumors of the ovary associated with ascites and pleural effusion have been reported, but in all of these cases the ovarian tumor was a fibroma and the presenting symptom in the majority was respiratory distress. In the present case the presenting symptoms which required relief were dyspnea and enlargement of the abdomen. Also in this case carcinomatous degeneration existed, but as far as known had not metastasized, nor was the pleural effusion due to secondary metastases. The author feels that these exceptions should be included in Meigs' syndrome, as they seem to present the same features and respond in the same manner when removed as do the ovarian fibromata.

(Either this paper was written a considerable time before its publication or else the search of the literature was incomplete, since the Meigs' syndrome has been described, not only with fibroma of the ovary, but with various other ovarian tumor types (carcinoma, granulosa cell tumor, thecoma, Brenner tumor).—Ed.)

There was no accompanying nausea or vomiting. A thick, tenacious vaginal discharge was noted. Menstrual periods had been normal and regular until the last, which had been missed. When seen in the hospital, the patient was in acute distress. Inspection of the abdomen revealed a slight elevation just to the left of the umbilicus. On palpation there was marked tenderness about the umbilicus and a mass, about the size of a lemon, was felt in this area. Dullness percussed in both flanks. On pelvic examination no glands were palpated. Cervix extremely soft and deviated to the left vaginal wall. Fundus of uterus pushed to right. Left adnexa presented a small tumor in the region of the left ovary. During pelvic examination the patient experienced for the first time a burning pain in the left shoulder, with shortness of breath and pain on breathing.

It was decided to do a laparotomy. Upon opening the abdominal cavity, a considerable amount of free blood was found and suctioned out. Right tube and ovary normal. Left ovary enlarged, with evidence of hemorrhage on its medial aspect. It was connected with the uterus by the ovarian ligament. The tube was entirely discrete from the ovary. The surface of the tube was smooth and not injected; the fimbriated end was normal. The tube was not removed, but the ovary was.

Examination of the ovary microscopically showed fragments of placental tissue. There was a defect on the surface, which was lined in part by large irregular cells containing irregular nuclei, resembling syncytial cells. Another section of the ovary presented a large intact corpus luteum. Here, also, were seen groups of cells resembling Langhans' cells. Some few appeared to be syncytial cells. There was some hemorrhagic extravasation in the adjacent tissue. Pathological diagnosis was (1) ruptured ovarian pregnancy; (2) corpus luteum of pregnancy.

Three figures.

(Although there is no direct evidence on the point, it would seem almost certain that a considerable number of spermatozoa must traverse the tube and make contact with the ovary, and yet ovarian pregnancy, as the authors state, is relatively rare. The logical explanation for this would seem to be that the ova as they exist in the ovary are immature and therefore not capable of fertilization. The first polar body is probably thrown off in the ovary, but the second is believed to be extruded in the outer portion of the tube. This same immaturity of the ovum probably explains the usual failure of cornual implantations of the ovary. That in rare cases maturation may be completed in the ovary is indicated by the rare occurrence of ovarian pregnancy and the occasional success with cornual pregnancy.—Ed.)

million and the hemoglobin to 5 Gm. She had been greatly debilitated. Treatment of the anemia was greatly handicapped by the fact that the patient was Rh negative, had panagglutinins in her blood and became jaundiced after any transfusion given her.

When the patient came under the authors' care at the Vanderbilt University Hospital in 1942, she appeared chronically ill. Her skin showed the changes of dermatomyositis. On pelvic examination a mass was felt which was thought to be a uterine fibroid. Her red blood cell count was 2.04 million, composed largely of spherocytes; the white cell count was 5,500 with a normal differential; hemoglobin was 7.5 Gm. She was Rh negative. After attempts to find compatible blood for transfusion failed, and the patient became increasingly anemic (17 days after admission the red cell count had dropped to 1.93 million, with a hemoglobin of 5.8 Gm.), an exploratory laparotomy was done. A large right ovarian cystic tumor (later found to be a pseudomucinous cystadenocarcinoma) was removed and the small intestine was freed from a large fibrous capsule. During the first five postoperative days three transfusions of plasma were given without reaction, but no whole blood transfusions were attempted. Within 26 days the red cell count rose to 3.97 million and the hemoglobin to 8.5 Gm., and the patient was discharged much improved. No spherical erythrocytes were seen. About six months later she was operated upon for an acute intestinal obstruction. Red blood cell counts on admission and discharge were 3.30 and 3.337 million, respectively, and hemoglobin contents, 11.8 and 9 Gm., respectively. This appears to be the first instance reported in which removal of an ovarian tumor alone was sufficient to effect pronounced improvement in a hemolytic process.

The authors offer the suggestion that some material elaborated by the ovarian tumor acted as a hemolysin; and refer to two other reports recording relief of hemolytic anemia following removal of an ovarian tumor.

## OVARIAN PREGNANCY

J. B. BALLINA AND N. E. CHIODI

Am. J. Obst. & Gyn., 50: 456-58, October, 1945

Because of its rarity, ovarian pregnancy is of great interest. The number of proved reported cases is very small. The case described in this article seemed to the authors to fulfill the criteria of Spiegelberg. In this case the Fallopian tube was not removed, since it was not edematous or injected and in no way connected with the ovary.

The reported case was that of a 26 year old woman, admitted to the hospital with the diagnosis of ruptured ectopic pregnancy. The morning of admission she had been seized with severe, sharp pain just to the left of the umbilicus.

hysterectomy and bilateral salpingo-oophorectomy is the operation of choice in the case of older patients who have theca cell tumors of the ovary. From this study they also conclude that postoperative roentgen therapy is indicated only in those cases in which carcinoma involves the cervix or the fundus of the uterus.

(A good review, and valuable especially because it is one of the few reports of end results in the treatment of thecoma. Such reports are almost as few regarding the much more numerous sister type of tumor, the granulosa cell carcinoma. Since no recurrence had occurred in the 20 cases of this series, one would have the impression that their malignant potentiality is less than that of the granulosa tumors. In the older group of patients radical operation is the proper plan, not merely because of the possibility of associated uterine carcinoma (the numerical incidence of this association is not really very high), but because of the malignant potentialities of the tumors themselves, admitting that they are far less wicked than ovarian cancer in general.—Ed.)

## MESENTERIC THROMBOSIS COMPLICATED BY DERMOID CYST

RUTH ELLIS LESH

Am. J. Obst. & Gynec., 50: 422-26, October, 1945

This article presents a case history and a brief summary of the literature regarding mesenteric thrombosis. Although this disease is relatively rare, the cases are important out of proportion to their number, because of their severity and grave prognosis.

Early diagnosis is made difficult by the fact that the symptoms can be those of other abdominal emergencies. However, a few symptoms occurring in practically all recorded cases sufficiently suggest occlusion of a mesenteric vessel as to warrant correct diagnosis. The typical symptoms of mesenteric thrombosis are described.

One case is reported, that of a 39 year old woman. Pain in the lower left abdomen began suddenly. Nausea and vomiting ensued. Pulse did not indicate shock. No relief from morphia or other drugs. Patient had been married 16 years; two children. For two years had been extremely nervous and morose. Sixteen years before right ovary, tube and appendix removed. Menstruation regular. On examination face was colorless. Heart sounds slow, weak and poor quality. Respirations 25. No mass palpable in abdomen, but extreme tenderness in lower portion, particularly on the left. Four hours after onset became shocked, with almost imperceptible pulse. On admission to hospital R.B.C. 4,030,000; leucocytes 15,050. Abdomen had become rigid in lower quadrants, and a definite mass was palpable in the left lower quadrant, extending above the symphysis. On vaginal examination a mass was felt in the left fornix. Differential diagnosis made of ovarian cyst with twisted pedicle or ruptured ectopic pregnancy.

# THECA CELL TUMORS OF THE OVARY. A CLINICAL AND PATHOLOGIC STUDY OF TWENTY-THREE CASES (INCLUDING THIRTEEN NEW CASES) WITH A REVIEW

EDWARD A. BANNER AND MALCOLM B. DOCKERTY

Surg., Gynec., & Obst., 81: 234-242, 1945

Data on 23 cases of theca cell tumor seen and studied at the Mayo Clinic during the period 1910-1944, inclusive, are presented with a correlation of clinical, pathologic, and chemical data. Ten of these cases had been reported by the junior author in the *American Journal of Obstetrics* in 1940 but have been re-examined in the light of more recent observations in staining reactions and of chemical assays of lipid substance as applied to tumors of this type.

From this investigation it appears that these tumors are derived from the ovarian mesenchyma and are closely related to the granulosa cell group of tumors. Occasionally the relationship may be a histologic one with elements of both types discernible with the same neoplasm, but usually both tumors present a "purity" of type. The relatively high incidence, especially in postmenopausal patients, of associated myometrial hypertrophy and uterine fibromyomas, combined frequently with endometrial hyperplasia and cervical and fundal carcinoma, suggests the production by the ovarian tumors of estrogenic hormone. Inability to demonstrate measurable quantities of this hormone through assays of tumor tissue is perhaps not to be regarded as conclusive evidence of absence of the hormone. A chemical analysis of 8 theca cell tumors gave evidence that these tumors contained increased amounts of cholesterol (0.2-1.8%) and cholesterol ester (trace-1.0%) fractions, as compared with the values (0.18-0.34% and trace, respectively) for these substances found present in 7 normal ovaries.

Although the tumors did not invariably produce clear-cut clinical symptoms, their presence could often be suspected by an alteration in the menstrual habits of the patient. Postmenopausal bleeding from a hypertrophic endometrium was commonly encountered in this series of patients.

In spite of the employment of new stains, the authors encountered difficulty in distinguishing certain fatty fibromas from theca cell tumor histologically. In such doubtful cases, examination of the endometrium was often found of value.

Follow-up studies made on 20 of these patients revealed that not one had died as a result of a malignant process beginning in a theca cell tumor. Seven had died from causes apparently not related to their ovarian tumors. Thirteen were living at the time of follow-up and had been well for postoperative periods varying from 6 months to 33 years. The authors conclude that surgical treatment in cases of theca cell tumor need be directed along radical lines only because of associated lesions, such as uterine fibromyomas and endometrial carcinoma, and not because of any malignant potentialities inherent in the theca cell tumor itself. Since, however, the incidence of associated uterine carcinoma is so high among postmenopausal patients who have theca cell tumors, they believe that

formed on March 23, 1944, the tumor being the size of a full-size rugby football after removal. The right ovary and uterus were conserved. There were no adhesions.

Gross and histological appearances.—The tumor which weighed 1,320 Gm. (about 3 lb.) was contained within a thick-walled capsule and had a variegated, lobulated appearance; small areas of cystic degeneration were present. The gross appearances corresponded with those of a solid ovarian teratoma. Similar tumors weighing up to 25 kg. (about 55 lb.) have been recorded. In the tumor the following types of tissue were observed: Squamous epithelium and keratin; hair follicles and sebaceous glands; fat and fibrous tissue; muscle bundles; cartilage and bone; blood-vessels and lymphoid tissue; salivary gland tissue; secreting glandular tissue resembling mammary gland; tall mucus-secreting epithelium resembling large intestine; tall ciliated columnar epithelium resembling bronchial mucosa; nervous tissue resembling brain tissue; other epithelial tissue unidentified, some of which resembles fallopian tube.

Pathologists such as Bland-Sutton, Ewing, Boyd, Beattie and Dickson state that these rarest of all ovarian tumors are malignant from the start and that they grow with extreme rapidity producing metastases of embryonic tissue that are sarcomatous in type. Gynecologists are, however, divided in their opinion as to the correct surgical procedure, for whereas Frank records a mortality of 88.8% within a year of operation, Curtis of Chicago states that 27% recover completely without hazard. Wilfred Shaw considers that at least 20% are innocent.

Hartman, Fraenkel, Williams and Chipman consider that if the patient is young, the ovarian capsule intact and the other ovary healthy, conservative surgery should be advocated; whereas Graves, Frank and Bonney advise complete extirpation of the uterus and both ovaries whatever the age and condition present.

Judging by the long experience of one of the authors (V. B. G.-A.) and that of H. R. Spencer, these cases are very rare. In the first case operated upon by one of the authors (V. B. G.-A.), he removed uterus and both ovaries and the patient succumbed from pulmonary metastases in seven months time. This present case has not been watched long enough to assess the result of conservative measures.

Postscript (May 12, 1944).—Patient's condition is satisfactory.

The authors then summarize certain aspects of our knowledge of these tumors as follows: cystic dermoid and solid teratoma of the ovary together appear to constitute about 10% of all ovarian tumors; the solid teratomas being very much the less frequent. Cystic dermoids and solid teratomas probably have an identical origin and appear to represent the extremes of a series of tumors arising from a common source. The cystic dermoid is initially benign and may rarely become carcinomatous; the solid teratoma is generally regarded as malignant from the start; the intermediate types are less or more liable to be malignant according to their position in the series.

The solid ovarian teratomas are of complex structure in which elements of all

Laparotomy performed. A small amount of serosanguinous fluid was encountered, and a gangrenous loop of ileum presented. About 48 inches of gut was excised and a V-shaped section of mesentery. Left tube and ovary appeared normal, except for adhesions. Pathological report showed a hemorrhagic infarction of intestine.

Patient had a stormy postoperative course, but was finally discharged on the fifty-third postoperative day, at which time the wound still drained from fecal material. The fecal fistula closed two weeks later.

Pelvic examination two months afterward disclosed a large mass in the pelvis. No symptoms referable to the growth, although patient said in a month she had gained weight rapidly. Menstrual periods and bowels normal. Mass enlarged steadily and in two months the patient was again admitted to the hospital and operation performed. A large dermoid cyst, containing cheesy material and hair, was found supplanting the left ovary and adherent to uterus, tube, omentum and intestines. In freeing the cyst a large abscess cavity, posterior and to the right, was entered, and drained. Postoperative course was uneventful, patient leaving the hospital in fourteen days. Three months following this operation she seemed entirely well.

The above case was offered to emphasize the symptoms common to such cases and to state the author's belief that surgical treatment without delay will lower the mortality. In the cited case, the author considers the most likely cause of the mesenteric thrombosis to be the fact that patient had entered the age of degenerative disease and that she had been under emotional strain for two years. The occurrence of the cyst was probably unrelated to the thrombosis, but perhaps elements contributing to the growth of the cyst were present in sufficient amount at the time of the first operation to have been the causative factor in the formation of the embolus. 16 refs.

(The dermoid cyst in this case was quite surely not related to the mesenteric occlusion, its chief importance being that the pelvic mass, and not unnaturally, obscured the preoperative diagnosis.—Ed.)

## A SOLID OVARIAN TERATOMA: CASE REPORT

V. B. GREEN-ARMYTAGE AND R. G. L. WALLER

Proc. Roy. Soc. Med. (Sect. Obst. & Gyn.), 37: 435-436, June, 1944

The patient, age 20, was sent to the West London Hospital on February 11, 1944, complaining of an abdominal tumor the size of a seven months pregnancy and two months' amenorrhea. The breasts were active but examination, auscultation, X-rays and a negative Aschheim-Zondek test eliminated pregnancy. The mottled appearance of the radiograph together with the ascites present suggested the preoperative diagnosis of teratoma. Left ovariectomy was per-

complained of menorrhagia and occasional intermenstrual bleeding. The last period began on March 26, 1942.

March 27, 1942: Examination under anesthesia. The uterus was bulky and a small swelling was felt in the left ovary. Curettings were profuse and the case was thought to be one of metropathia hemorrhagica with an ovarian retention cyst. Radium (3,000 mg. hrs.) was inserted into the uterine cavity. Section of the curettings showed a hypertrophic endometrium in the secretory phase.

June 23, 1942: The patient readmitted complaining of continuous bleeding since the insertion of radium.

June 26, 1942: Laparotomy. The uterus appeared normal. There was a small solid tumor in the left ovary. Total hysterectomy, bilateral salpingo-oophorectomy and appendectomy performed.

The convalescence was uneventful and the patient is now well.

Specimen.—Uterus slightly bulky with a small submucous fibroid.

There was a small solid tumor in the left ovary  $1\frac{1}{2}$  in. by 1 in., which resembled a fibroma but with the characteristic yellowish areas. The right ovary was normal.

Sections of the uterine wall showed degeneration and atrophy of the endometrium. The ovarian tumor was a typical thecoma and a section stained for fat showed the characteristic droplets in the epithelioid cells.

Nature and origin of the tumor.—Novak (1940) believes these tumors are granulosa-cell tumors which have undergone luteinization. Schiller (1940) places the thecoma in the groups of tumors which arise from the ovarian mesenchyme and classified them as a subgroup of the fibromata of the ovary. It is not possible at present to decide which of these views is correct, but there seems to be some ground for regarding the thecoma as a separate pathological and clinical entity. Traut and Butterworth (1937) were able to produce thecomata and granulosa-cell tumors in immature mice by irradiation of the ovaries, thus suggesting that the origin of the two groups of tumor is similar.

The interest of the case reported above lies in the presence of a comparatively rare ovarian tumor and in the persistence of uterine bleeding in spite of the atrophy of the endometrium caused by radium. It is suggested that in all cases of fibroma of the ovary, especially if there has been an irregular uterine hemorrhage, a section of the tumor should be stained for fat. It is probable that this tumor is much commoner than the reports would suggest.

(There is still a tendency, it seems to me, to take granulosa cell and theca cell tumors too lightly from the standpoint of malignant potentialities. Granted that their malignant propensities are far less than those of the more common primary types of ovarian cancer, many cases in the literature emphasize that recurrence, metastasis and a fatal termination occur in a considerable number, and this may be true even when radical operations have been done. Although this group of tumors has been recognized for now many years, there is still a paucity of reports as to the ultimate results in large groups of these cases, although no doubt a better crystallization of opinion on this point will be possible before many more years.

In most cases of thecoma, as in the one reported by Barnes, there is an admixture of epithelial (granulosa) or epithelioid cells, pointing strongly to their close kinship and to

organs have at one time or another been identified. These elements of the various tissues of the body are mixed indiscriminately without any attempt at formation of complete organs. The degree of malignancy in the series of tumors appears to be dependent upon the extent of differentiation or absence of differentiation into completed organs.

Owing to the absence of differentiation, this present tumor must be regarded as malignant and liable to give rise to metastases of a sarcomatous or undifferentiated embryonal type via the blood-stream, chiefly in the lungs and liver. Perforation of the capsule does not appear to have occurred in this case, so that direct extension or implants within the pelvic or abdominal cavities are unlikely.

(The English source of this report is amusingly manifest in that the tumor is described as having the size of a "full-size rugby football." Could you imagine such a comparison in an American paper?

As the senior author has found in his long and rich experience in gynecological practice, these tumors are very rare, which may seem rather surprising in view of the frequency of their benign prototype, the common dermoid cyst. It is not strange that there are not more studies as to their degree of malignancy. That this is high, there can be no doubt on the basis of individual case reports. Even the most radical operations have often been followed by rapid metastases, as in the case mentioned by Green-Armytage from his early experience, and most gynecologists will probably hesitate to perform conservative operations in the removal of such tumor, in spite of the unfortunate fact that this tumor is characteristically found in young women and often in children.—Ed.)

## THECOMA OF OVARY: CASE REPORT

JOSEPHINE BARNES

Proc. Roy. Soc. Med. (Sect. Obst. & Gyn.), 36: 364, May, 1943

The tumor commonly known as thecoma of the ovary was first described in 1927 by two Italians, Moretti and Arrigoni, who named it "fibroma thecocellulare xanthomatodes ovarii."

The tumor occurs mainly in women who have passed the menopause, though several of the reported cases have occurred in younger women. It may cause menstrual irregularity or post-menopausal bleeding. It is always unilateral and is a solid tumor, consisting of connective tissue cells, surrounding islets of more deeply staining cells, which in suitably stained sections will be seen to be laden with fat droplets. These cells may be epithelioid or spindle-shaped. Wolfe and Negus (1941) were able to demonstrate that these fats are mainly cholesterol and phospholipoids. Geist and Spielman (1935) showed that the tumor contained estrogenic hormone, and, using castrated mice, were able to show that the amount exceeds that found in an equivalent weight of placental tissue.

Malignancy is rare and unilateral oophorectomy is often the only treatment required.

Case report: The patient was aged 48 and had had eleven children. She

this paper is to illustrate that intensive irradiation in this patient at the age of four and a half had not destroyed ovarian function, since she began to menstruate normally at 12 and continued to the age of 19. This is of interest, especially since there are so few observations as to the effect of irradiation on the ovaries of subpuberal girls. However, it is a well-known fact that during reproductive life ovarian function is at times permanently abolished by far less intensive treatment than was employed in this girl, while in other patients, as illustrated in the irradiation induction of the menopause for functional bleeding, the ovarian secretory function seems very hard to kill. In other words, there are very wide differences in the degree of responsiveness of individual ovaries to either X-ray or radium.

The particular point of discussion has been as to the safety of the "stimulating" radiation treatment of the ovary, the pituitary, or both for the often refractory cases of amenorrhea and sterility, to mention the two chief indications for which it has been employed. Some, like Kaplan, have reported good results, with apparently little or no harmful effect. Others, including the majority of conservative gynecologists, are apprehensive as to possible injurious effects upon the germ cells, with the possible production of defects in the ova, resulting in later sterility, miscarriage or the birth of defective children. It must be admitted that there is no very convincing evidence of such serious results in humans, but geneticists like Little have apparently shown that the danger is a real one in the experimental animal. Nor are the clinical results obtained by this method uniformly good, nor anything like as good in the experience of other observers as those reported by the few enthusiasts for the method. Some who formerly employed it rather enthusiastically have abandoned its use. It is probable that the majority of gynecologists will continue their conservative attitude toward this method, at least until the evidence for its value and its harmlessness are more sharply crystallized than they are at present.—Ed.)

## PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

R. M. MITCHELL AND R. W. MOHLER

Am. J. Obst. & Gynec., 50: 283-92, September, 1945

The objective of this article is threefold: (1) to submit a case report of primary carcinoma of the Fallopian tube discovered on routine microscopic examination of segments removed at the time of an elective cesarean section; (2) to bring the literature up to date as far as possible; and (3) to mention briefly again the salient points regarding primary carcinoma of the Fallopian tube, even though this case is not entirely comparable with respect to diagnosis, since it was accidentally rather than preoperatively suspected.

To date, some 449 cases of this disease have been recorded. Its frequency rate among tumors of the genital tract averages about 0.5 per cent. Age apparently has no effect on the disease, although the greatest incidence is in the fifth decade. Unilateral involvement occurs in 70 per cent of cases and bilateral lesions in 30 per cent. Secondary carcinoma of the Fallopian tube is ten times as frequent as primary carcinoma.

Although the etiologic factor is unknown, several investigators believe that inflammatory pelvic disease predisposes to its occurrence, and Fullerton states that the frequency of coincident tuberculosis may be of importance.

their common origin from the ovarian mesenchyme. It is this viewpoint which I have myself urged and not, as the author very wrongly quotes me, that thecomas are "granulosa-cell tumors which have undergone luteinization." Tumors of the latter group are of course not thecomas, and they constitute an entirely different variety, the so-called "folliculome lipidique."—Ed.)

## THE EFFECT OF IRRADIATION ON THE FUNCTION OF THE OVARY IN YOUNG GIRLS

IRA I. KAPLAN

Am. J. Obst. & Gynec., 50: 340-41, September, 1945

In 1939 the author reported the case of a young girl who received intensive irradiation, x-ray and radium treatments for a pelvic tumor at the age of 4½ years, and who nevertheless menstruated normally from the age of 12 to 19 years. The purpose of that report was to show that unwarranted apprehension was present in the minds of clinicians in regard to the effect of irradiation in girls and young women. In this paper he presents the unfortunate conclusion of the case.

The patient reported to the author on July 2, 1943, complaining of a painful area on the right side of the coccyx of about 6 months duration. An extremely tender, firm, regular, round nodule was found at the base of the spine to the outer border at the gluteal margin. It was not attached to the skin, not too firmly attached to the underlying tissues, and was not compressible. X-ray therapy was administered with apparent relief of symptoms.

Several months later she reported increasing pain at the coccyx area on sitting down. Examination revealed persistence of the tumor which was then removed by surgery. Pathologically the neoplasm proved to be a neurogenic type tumor. Temporary relief was obtained until recurrent pains became very distressing and x-ray therapy was given, failing to bring relief. Three months later x-ray was again instituted. In April, 1944 she was examined and a large tumor felt through the rectum firmly filling the right pelvis. She was operated upon but the tumor could not possibly be removed. Microscopic examination showed that the tumor was a ganglioneuroma that had undergone malignant neurinoma changes (neurogenic sarcoma, graded I). The wound failed to heal and another piece of tissue, removed in May, 1944, was examined and the diagnosis made of spindle-cell sarcoma, neurogenic type, of buttock.

The patient died, in spite of all measures taken, in September, 1944. Autopsy revealed the tumor fixed to the rectal wall by its capsule and bulging into the pelvis. The exposed portion revealed large areas of dirty grayish necrosis and adjacent areas of hyperemia and hemorrhage. 1 reference.

(The author has been an enthusiast in the treatment of such endocrinopathies as amenorrhea and certain cases of sterility by light irradiation of the ovaries, and the purpose of

of the papillary variety. Although the microscopic report revealed that the lesion had been removed in its entirety at the time the sterilization was done, in view of the unfavorable prognosis for this disease, complete extirpation of the uterus, tubes and ovaries was considered imperative. 44 references.

(The interesting case reported in this paper represents a "lucky find," but a find which would not have been yielded except for the routine examination of all removed tissues, the importance of which the authors properly emphasize. The follow-up of this case should be of great interest. The prognosis should certainly be far better than in most cases of primary tubal carcinoma, because the disease is such an insidious one that most of the reported cases have come to treatment in late stages. As a matter of fact, it is quite probable that it is this very insidiousness, with the lack of any symptoms until late stages, which has given this disease its wicked reputation even more than its own intrinsic characteristics, bad as these themselves may be.

Not all will agree, therefore, that primary carcinoma of the tube is the most malignant form of carcinoma anywhere in the body; and that, for example, it is as hopeless as melanomas, primary carcinomas of the liver, and certain other types of cancer, though this is a very minor point for discussion. The paper includes a comprehensive and useful review of the literature of this very rare but highly malignant disease.—Ed.)

## PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

J. ERNEST AYRE, W. A. G. BAULD AND P. J. KEARNS

Am. J. Obst. & Gynec., 50: 196-202, 1945

The case of primary bilateral carcinoma of the tubes presented in this paper presents several points of interest. The tissues appeared generally quite clear-cut and free from extensive necrotic degeneration which might otherwise have destroyed the cytology. Some sections presented a papillary appearance, others a pseudoglandular or alveolar appearance. A second smaller tumor presented a definitely solid structure. It thus appears that not three independent types of tubal carcinoma (papillary, alveolar, and solid) are represented, but that these are merely local variations in morphology. These findings were obtained after panhysterectomy. Except for the presence of one or two marble-sized fibroids on the posterior surface of the uterus, the other pelvic organs appeared normal. The difficulties encountered in diagnosing tubal carcinoma clinically, the infrequency with which it is encountered at operation, and the extremely high mortality associated with it are discussed.

(The authors believe, as do many others, that the various histological types of primary tubal carcinoma which have been described, viz., the papillary, the alveolar and the solid are actually only local variants of one type. Their photomicrographs, taken from different parts of the same tumor, appear to support this view. In their paper they discuss the belief held by some that salpingitis is a predisposing factor in the development of tubal cancer, which would seem unlikely in view of the very great frequency of inflammatory lesions of the tube and the extreme rarity of tubal cancer. They themselves are more inclined to the belief that associated inflammatory reactions in the carcinomatous tube are to be explained as a result of the malignant growth.—Ed.)

The most frequent site is the distal two-thirds of the organ. McGoldrick et al. state that there are two kinds: the papillary, growing into the lumen of the tube and the infiltrative, growing into the tubal wall. Invasion of the tubal wall is usually a late occurrence or may be absent. Metastases have been found in the reproductive and urinary tracts and in the liver, lungs, stomach, large intestines, diaphragm, spleen, skin and supraclavicular nodes long before the tubal wall has been involved.

Bleeding is the earliest and most important symptom. The symptom complex of pain associated with gushing of water, yellow or bloody fluid from the vagina followed by relief of pain is known as "hydrops tubae profluens" and is suggestive of carcinoma of the Fallopian tube. There may be disturbance of menstrual function or postmenopausal bleeding.

Preoperative diagnosis is difficult but tubal carcinoma may be suspected where bleeding has recurred after a negative curettage of an atrophic uterus.

The usually accepted form of treatment is total hysterectomy and bilateral salpingo-oophorectomy, with postoperative roentgen therapy in some cases. A normal-appearing opposite tube should not prevent radical procedure, since 30 per cent of the reported cases are bilateral. Carcinoma of the tube is the most malignant form of carcinoma anywhere in the body and according to Fullerton, not more than 5 per cent of patients get a five-year cure.

The case reported is that of a 23-year-old white woman who first registered at the Out-Patient Department of the Lying-in Division of the Pennsylvania Hospital in June, 1940. Her prenatal course was uneventful and she was delivered in March, 1941 of a normal full-term infant. The postpartum course was normal. She again registered in May, 1942 and this pregnancy was interrupted by an emergency classical cesarean section for central placenta praevia in October, 1942. She was discharged twelve days postoperatively in good condition. She was next seen in July, 1943, two months pregnant, with a negative interval history. In February, 1944 she received an elective cesarean and sterilization. The tubes were ligated and resected and specimens of the resected tubes were sent to the laboratory for routine confirmation. The pathological diagnosis was as follows: "Segments of Fallopian tubes: one segment appears normal, the other segment shows primary carcinoma and both segments show pregnancy changes consisting of swollen smooth muscle fibers."

In view of these findings, the patient was subjected to a total hysterectomy and bilateral salpingo-oophorectomy. The patient's postoperative course was normal and three months later she appeared entirely well. Six months after her physical examination was negative and she had gained six pounds. Deep roentgen therapy has been instituted.

Interesting features in this case are: (1) the accidental discovery of the tumor; (2) the occurrence of primary carcinoma of the Fallopian tube with a normal intrauterine gestation at term; (3) the histo-pathologic study; and (4) the importance of a routine pathologic examination of tissues.

Whether the tumor was originally a benign papilloma stimulated to growth by the effects of gestation is conjectural. The tumor appeared to be characteristic

of the fallopian tube, though Doran, in 1896, mentioned an unreported case of Raynaud's from 1847, while in 1861, Rokitansky gave the first pathological description of this disease.

The most recent review is by H. J. Baron (*Canad. Med. Ass. J.*, 1940, 43: 118-121), when he brought the total number of cases to 363, since when the present author has been able to find a further 15 in the literature. This disease is most common between the ages of 40 and 55, though cases have occurred in a girl of 18 and a patient of 73.

Symptoms are few, the most important being a slight watery, sometimes pink-stained, discharge. This may occur at intervals and is associated with attacks of colicky low abdominal pain, when the distended tube may empty its contents into the uterus.

The diagnosis has only been made pre-operatively on one occasion. However, the combination of a discharge of that character without uterine abnormality but accompanied by an adnexal enlargement, might suggest a tubal carcinoma.

(The statement that during operation a "friable, papilliferous mass, the size of a golf-ball, fell out of the tubal orifice," is of interest, as emphasizing the characteristic concentric or intratubal mode of growth of primary tubal carcinoma. In the more advanced stages, such tumors convert the tube into a large sausage-like mass looking like a large pyosalpinx, except that often the tubal mass may be quite free, without the dense adhesions ordinarily characterizing the pyosalpinx. On cutting across the tube in such a case, the tubal wall itself is often very thin, but the lumen is filled with a crumbling papillary mass, as in the case described by the author. In his case, an incomplete operation was done, and the ultimate prognosis is very poor, in spite of the fact that the patient seemed well four months after operation. For that matter, it would probably have been bad even with complete operation, in view of the usual experience with primary tubal carcinoma.—Ed.)

## PRIMARY SARCOMA OF FALLOPIAN TUBE: CASE REPORT

BRAITHWAITE RICKFORD

*Proc. Roy. Soc. Med. (Sect. Obst. & Gyn.)*, 38: 322-323, May, 1945

The patient, aged 69, on August 16, 1944 complained of vaginal discharge for two months. The previous history was not significant. Menstruation had started at 15 and had always been normal. The menopause had occurred nineteen years ago when menstruation ceased suddenly and there had been no further loss or discharge until the onset last year. There had been two children without any abnormalities, the last thirty-two years ago. One miscarriage had occurred which had required evacuation of the uterus.

A heavy vaginal discharge had been present for two months which required two to four diapers a day. It was rather thick, whitish in color, and often definitely pink-stained. There had never been any frank bleeding, and it had never been offensive. There was no pruritus, pain or discomfort anywhere.

## PRIMARY CARCINOMA OF FALLOPIAN TUBE: CASE REPORT

BRAITHWAITE RICKFORD

Proc. Roy. Soc. Med. (Sect. Obst. &amp; Gyn.), 38: 322, May, 1945

The patient, aged 36, was first seen on October 25, 1944, complaining of sterility. Twenty-four years previously she had had an acute appendicitis with a pelvic abscess, which had necessitated her being in the hospital for nine months. She had been married for six years, her husband had been at home throughout and on investigation had been found to be fertile.

Her menstrual history was quite normal, starting at the age of 15, and was regular. She had noticed some vaginal discharge for the previous ten years, which was most marked for the seven days following menstruation.

On examination she was a healthy patient, not anemic, and was of average weight. The abdomen showed a firm tumor in the midline, reaching about 1 inch above the symphysis pubis. It arose from the pelvis and was slightly mobile. Otherwise there was nothing of note on abdominal examination. Vaginal examination showed that this tumor was in the uterus, which was regularly enlarged to the size of about a fourteen weeks' pregnancy. It was hard in consistency and mobility was limited. To the right of the uterus and posteriorly was another tumor, which was rather softer and apparently attached to the uterus.

Laparotomy was performed following an unsuccessful attempt at insufflation. The intestines were thickly adherent to each other and to the pelvic organs, with dense matted felty adhesions. It was impossible to recognize the uterus or appendages on inspection. The uterus, however, was palpated and found to contain a hard tumor in the anterior wall. To the right of the uterus was a softer mass, which appeared through the adhesions to be of a bluish-brown color, rather resembling that of a tubal abortion. This mass was separated digitally and during this process a friable papilliferous mass, the size of a golf ball, fell out of the tubal orifice. Surrounding the mass was a collection of thick, blood-stained glairy mucus. The right tube was then removed, the ovary being left in situ, and apparently normal. The left adnexa were palpated through the adhesions and were apparently normal. A myomectomy was then carried out for an interstitial fibroid after dissecting blindly through the adhesions covering the anterior wall of the uterus. Hemostasis was not absolute and the abdomen was closed with a tube drain for forty-eight hours.

Convalescence was uneventful and a full course of deep x-ray treatment to the right posterior quadrant of the pelvis was instituted sixteen days later and completed in twenty-eight days.

Four months later the patient was extremely well and pelvic examination revealed no abnormality. Menstruation had occurred once since operation.

Pathology: "Papillary columnar-cell carcinoma of the fallopian tube."

Orthmann, in 1886, reported the first authenticated case of primary carcinoma

## COCCIDIOIDAL PELVIC INFLAMMATORY DISEASE

ERNEST W. PAGE AND L. MORGAN BOYERS

Am. J. Obst. &amp; Gynec., 50: 212-215, 1945

This is the second case of infection of the female genital tract with *Coccidioides immitis* reported in the literature. In the first case, recovery of the patient was attributed to the use of a coccidioidin vaccine and colloidal copper. In the present instance, surgical removal of the involved organs (uterus, tubes and one ovary), followed by no "specific" treatment, effected a complete cure. The patient probably acquired the infection while digging ruins in the Arizona desert.

She was feeling very well in herself, there had been no loss of weight or anorexia. The bladder and renal functions were normal.

On examination the patient was healthy, of average weight and not anemic. Abdomen was normal. On vaginal examination the cervix was small and atrophic, and a firm mass could be felt in the left posterior quadrant of the pelvis and was thought to originate from the uterus. On August 29, 1944 the cervix was dilated and the uterus measured only 2 inches. No curettings were obtained. Following this there was slight pyrexia associated with some lower abdominal pain for three weeks.

On November 3, 1944 laparotomy was done. No free fluid in the abdomen; a tumor about the size of a grapefruit was found in the left posterior quadrant of the pelvis which was adherent to the back of the uterus. It was found that the upper serous covering of the tumor was the grossly thinned wall of the distended left fallopian tube. The tumor had dilated the abdominal ostium and was attached directly to the posterior surface of this broad ligament and the uterus. It was removed in one piece with the tube. A considerable area of ragged, oozing tissue remained in the tumor bed. The abdomen was closed with a drain down to the pelvis. The left ovary was seen to be small and atrophic after the growth had been removed, while the right appendages were normal and the uterus was small and atrophic. No glandular involvement was found, and the omentum was free from secondaries, as was also the liver. The tumor after removal was brain-like in appearance. There were considerable areas of necrosis and hemorrhage with many small cystic spaces. The fallopian tube was grossly dilated in its upper two-thirds, with the tumor growing from its inner wall and through the abdominal ostium.

Convalescence was complicated by a small infarct of the lung sixteen days later, which rapidly resolved. A full course of deep X-ray treatment was given to the left side of the pelvis.

February 10, 1945: Patient very well; no abnormality in the pelvis.

Pathology: Spindle-cell sarcoma arising from the wall of the fallopian tube.

The first reported case of sarcoma of the fallopian tube was described by Sanger in 1886, and the most recent review of the literature is by Jorgensen (*Acta, obstet. gynec. scand.*, 1938, 18: 326). He reviews sixteen cases in all, the only previous English reference being by J. B. Banister, *Proc. R. Soc. Med.*, 1924, 17: Sect. Obstet., 31.

(This is an exceedingly rare tumor, as the author states, much more so even than the very rare carcinoma. We have observed only one case in our own laboratory.—Ed.)

1910, this later being modified by others, especially by Stoeckel in 1917 (the Goebell-Stoeckel operation). The recent publication of Aldridge (1942) reported excellent results from the use of transplanted strips obtained from the aponeurosis of the oblique muscles in combination with a plastic operation on the bladder neck and upper urethra (*Amer. J. Obst. & Gynec.*, 44: 398, 1942).

The two methods described by Studdiford, both utilizing lateral strips of the aponeurosis, are well illustrated by good line drawings, and the interested reader will have to be referred to the original paper for these operative details. In the limited group of patients for whom Studdiford advocates these procedures the anatomic and functional results obtained would seem to justify the principles on which the operations are based—Ed.

## CASE OF CONGENITAL ANOMALY OF THE FEMALE URETHRA AND VAGINA

C. C. HIGHTOWER

Mississippi Doctor, 23: 398, August, 1945

A 22-year-old woman came to the author with a history of never having menstruated normally. Each month she had a black discharge lasting two weeks accompanied by pelvic pains. She had been married two years and coitus was satisfactory. Vaginal examination showed that the vagina, normal in other respects, ended in a blind pouch. The uterus could be palpated on deep pressure. The urethra opened into the anterior vaginal wall near where the cervix should be.

At operation, when the black discharge was present, its source was discovered. There was a pin-point opening in the dome of the vagina. Upon dilating this opening with a small probe it was discovered that the vagina was divided into two parts by a septum. The septum was removed and a normal cervix and uterus found behind it. Nothing could be done with the abnormally situated urethra. Urination through the vagina seemed to cause no trouble before or after operation.

Since operation, the patient has menstruated normally and been cured of all dysmenorrhea. The dysmenorrhea was due to the fact that it required two weeks for the accumulated menstrual blood above the vaginal septum to pass through the minute opening in the septum.

(I have seen a number of cases in which the urethra opened on the anterior vaginal wall well within the introitus, but always in cases of pseudohermaphroditism in which the primitive and undeveloped vaginal canal joins the urethra at an acute angle some distance above the external orifice. By far the best source book for the embryological elucidation of the many possible anomalies in this region, is the monumental work of Robert Meyer on "Embryology of the Vagina."—Ed.)

## FEMALE UROLOGY

### FURTHER EXPERIENCES IN THE USE OF TRANSPLANTED ABDOMINAL FASCIA IN THE RELIEF OF STRESS INCONTINENCE

W. E. STUDDIFORD

Am. J. Obst. & Gynec., 50: 119-137, 1945

The anatomic basis for urethrocele and its associated symptom, stress incontinence, is reviewed and discussed briefly, together with the etiological factors which produce this condition. While incontinence of urine is a fairly common complaint in gynecological patients, it is usually so slight that it constitutes only a minor annoyance. However, it sometimes develops to such a degree that the patient discharges large quantities of urine upon the slightest muscular effort. It is with these extreme cases, particularly those in which previous efforts at relief have failed, that this paper is chiefly concerned. It is thought that the essential weakness lies not in the internal sphincter but in the supporting structures about the upper urethra and bladder neck, and that, therefore, the failures following the common type of surgical repair appear to be related to the attenuated character of the residual supporting tissue. Failures which follow the use of the transplanted tissue techniques may, in the author's opinion, be due to the fact that emphasis was placed on the substitution of voluntary muscle for a supposedly damaged internal sphincter rather than on the restoration of proper support. Two procedures, devised by the author, are described. Both of them utilize strips of abdominal aponeurosis in addition to plastic repair of the supports. The first method was used for patients in whom previous surgical efforts had failed; the second was utilized as a primary procedure in patients who had multiple complaints and required both plastic and abdominal surgery. Thirteen cases are reported in which these procedures had been used and follow-up to date of publication had not revealed a recurrent urethrocele or the reappearance of stress incontinence.

(In this excellent paper on "stress incontinence," a term said to have been coined by Eardley Holland, Studdiford emphasizes that his report is concerned chiefly with the extreme degrees, in which the patients are continent only on lying down or sitting quietly and, even under such circumstances there is lack of urinary control if the intra-abdominal pressure is raised. The mild cases are of minor consequence, and if any treatment is called for, may be cured by comparatively simple operations, such as those of the Kennedy type. The author believes that the good results reported by many from the Kelly operation of tightening the internal sphincter are to be explained by the unconscious inclusion in the Kelly stitch of the supporting tissues about the upper urethra and bladder neck.

He reviews the modern concept of the mechanism of urination, and also describes the supporting mechanism of the female urethra and bladder. For the extreme cases, in which a definite proportion of failures is inevitable with the simpler types of operation, a variety of more extensive procedures have been recommended, beginning with that of Goebell in

1910, this later being modified by others, especially by Stoeckel in 1917 (the Goebell-Stoeckel operation). The recent publication of Aldridge (1942) reported excellent results from the use of transplanted strips obtained from the aponeurosis of the oblique muscles in combination with a plastic operation on the bladder neck and upper urethra (*Amer. J. Obst. & Gynec.*, 44: 398, 1942).

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## A SERIES OF FORTY CASES OF VESICOVAGINAL FISTULA

G. BENION THOMAS

J. Obst. &amp; Gynec. Brit. Emp., 52: 262-70, June, 1945

In a study of the problem of vesicovaginal fistula, the author describes his experience in treating 40 cases, primarily by the flap method of operation. The fistulae are classified according to their situation as juxta-cervical, midvaginal or juxta-urethral, there being in this series, 18 juxta-cervical, 5 midvaginal and 17 juxta-urethral fistulae. Of these 40 cases, 35 submitted to treatment and 28 were cured, 25 by the flap method of operation and 3 by other means. There were two deaths from suppression of urine following transplantation of the ureters. Included in the 35 cases which submitted to treatment are 2 which were regarded as inoperable. Twenty of the 21 juxta-cervical and midvaginal cases submitting to operation were cured by the flap method at the first attempt. The juxta-urethral cases were less successful; of the 14 who agreed upon operation, the flap method was performed on 7 with 5 successes and 3 more cases were cured by other means, making a total of 8 cures.

Because the author used the flap operation most frequently and found it the most successful treatment, he describes it in some detail. He recommends that at least 3 months should have elapsed since the last labor or operation before attempting a repair. An intraspinal anesthetic of light percaïne is ideal and lasts sufficiently long. The surgical technique is explained with illustrations and advice as to after care is given. Other operations which were used are described: Bonney's operation for elongation of the urethra, sacculi operation, colpocleisis and transplantation of ureters.

The view is advanced that repair by the abdominal route is probably only rarely necessary. It was not required once in this series. Also, transplantation of the ureters rarely should be required and should be avoided if possible.

Classical cesarean section is advocated in all deliveries subsequent to operation upon vesicovaginal fistula. The descent of the head in vaginal deliveries is bound to stretch the scar of a healed fistula and considering the difficulties involved in so unfortunate an occurrence, classical cesarean section seems justifiable in all cases which one sees before labor begins and when considerations of sepsis do not prohibit. 6 references. 6 figures.

(Comment on this paper is made after the following abstract.)

## VESICOVAGINAL FISTULA

D. JOAN THOMPSON

J. Obst. &amp; Gynaec. Brit. Emp., 52: 271-77, June, 1945

In a total of about 80 cases of vesicovaginal fistula seen by the author, the cause in 3 cases was malignant disease. In the remainder, (about 95 per cent), the cause was faulty obstetrics.

In a series of 42 cases reviewed in this report, infection of the bladder was found in 18 cases, gonococcal infection in 5 and in all cases *Bact. coli* were present. In all infected or doubtful cases, preliminary treatment, usually with sulphonamides, was given.

Twenty-seven cases were treated by attempts at plastic repair. The results were: cured, 55.8 per cent; failed, 40.4 per cent; died, 3.8 per cent. Causes of inoperability were: size of fistula, difficulty of approach, destruction of the urethra, gross destruction of tissue and fistulae at the neck of the bladder with the urethra torn away. Causes of failure were: much scar tissue, especially in the bladder wall, infection and postoperative hemorrhage.

The most effective method of treating inoperable cases is by transplanting the ureters into the large bowel, usually the sigmoid colon. Oblique implantation is now generally considered to be the best. In this series, 13 cases were treated by ureterosigmoidostomy, 9 in 2 stages and 4 at a single operation. Eight patients were cured and 5 died. The two-stage operation is usually safer.

Of the 5 deaths, one was due to anesthetic; another patient developed a urinary fecal fistula with amoebic dysentery and a retroperitoneal abscess which proved fatal. A third died of urinary peritonitis due to careless technique. The other two deaths were in patients who had received 1-stage operations. One died of renal failure and the other of what appeared to be peritonitis.

Ureterosigmoidostomy is useless if there is a rectovaginal fistula or a tear of the sphincter muscle of the anus. 12 references.

(It is interesting to compare the opinions of the authors of the two preceding papers, both emanating from clinics in India, and also to compare their results. Those reported by Thompson seem less favorable than those of Thomas, but this may mean only a difference in the types and degrees of urinary fistulas treated. That the group reported by Thompson must have included many difficult cases is indicated by the fact that she felt impelled to resort to ureterosigmoidostomy in 13 of her 80 cases, and there will be general agreement that this plan is the most effective and about the only feasible one in the treatment of otherwise hopeless cases. On the other hand, no issue can be taken with Thomas' statement that transplantation of the ureters should only rarely be required and should be avoided if possible.

Fundamental as was Sims' original work on vesico-vaginal fistula, and valuable as the Sims operation still is in many of the simpler fistulas, great advances have been made since the time of Sims in the management of the more difficult fistulas, especially those of large size and those inaccessibly placed in the vault of the vagina. The important principle of free mobilization of the bladder before suture, and the employment of the Schuchardt incision in the highly and inaccessibly placed fistulas, have been especially valuable contribu-

tions. Rather paradoxically, the very low fistulas which involve destruction of the urethra still are bugbears, and their cure taxes the plastic skill of any gynecologist, with failure as a frequent result.

It is of interest to note that in Thompson's series, about 95 per cent were ascribed to faulty obstetrics. While this figure might have applied also to the American picture of a generation ago, it certainly does not apply now. This is to be explained only partly by the improvement in obstetrical care, since most of the fistulas now observed in this country are complications of operations, especially panhysterectomy and cystocele repairs of one sort or another, or of radiation therapy for malignant diseases.

As a final comment, the statement by Thomas that repair of fistula by the abdominal route is only rarely necessary may be heartily endorsed.—Ed.)

## PROLAPSE OF URETHRA IN A CHILD OF 6 YEARS: CASE REPORT

J. CHASSAR MOIR

Proc. Roy. Soc. Med. (Sect. Obst. & Gyn.), 37: 436-437, June, 1944

The patient, a healthy child of six years, suddenly started to bleed from the vulva. The mother saw what she took to be a large blood-clot at the entrance to the vagina. There was no previous history of bleeding or of bladder symptoms.

The next day the child was sent to the hospital. She complained of soreness, and there was still a slight loss of blood. A dark red, velvety mass nearly an inch in diameter, bulged through between the labia and obscured all the structures in that region. The author's house-surgeon—an experienced man—reported that he imagined that the child must be suffering from some rapidly growing, fungating sarcoma. An X-ray examination did not show any foreign body in the bladder.

Under anesthesia fuller examination was possible, and it became obvious that the condition was an extensive prolapse of the mucous membrane of the urethra. The passage into the bladder was situated at the posterior part of the mass. By firm, sustained pressure the mass was replaced. There was an obvious tendency to recurrence, and a catheter was therefore inserted into the bladder and secured in position with the hope that the constant pressure would prevent a renewed protrusion of the mucosa. This treatment was only partly successful; by next day, in spite of immobilizing the child as much as possible, the catheter became dislodged and the prolapse returned as before.

Two days later the child was again anesthetized. Four fine catgut stitches were inserted, flush with the fossa navicularis, passing from the outside to the urethra, and from urethra back to the starting point. The sutures were then tied, and the redundant mucosa excised. A catheter was not inserted. The child made an uninterrupted recovery, and at no time had she any difficulty with micturition. She has been seen again recently and it was not possible to detect any abnormality. Micturition is normal. On questioning, the mother states

that the child has some "urgency" but never wets herself, nor does she want to void urine unusually often.

Prolapse of the mucous membrane of the urethra is a rare condition and the author is not aware of any previous record of its occurrence in a child. It is probably associated with an unusually wide urethra; this seemed to be so in the case described.

The author speculates on how much mucosa can be drawn down and excised without interference with the bladder function. In this case the excision caused no appreciable ill-effect.

(Prolapse of the urethra is relatively rare at any age, and certainly extremely rare in children. I agree with Moir that resection of even considerable segments of the prolapsed mucosa rarely causes incontinence. In one instance which I have observed in a woman of 72, the prolapsed mucous membrane had become strangulated, being of blackish-blue, almost gangrenous appearance. Although at least 2 cm. of the mucosa was removed by the circumcision type of operation which was done, there was no interference with later urinary control.—Ed.)

## OPERATIVE GYNECOLOGY

### VAGINAL HYSTERECTOMY IN THE MANAGEMENT OF DESCENSUS UTERI

W. C. DANFORTH

Am. J. Obst. & Gynec., 50: 376-384, October, 1945

In the treatment of descensus uteri two procedures are at present employed almost to the exclusion of other methods. One is vaginal hysterectomy, with the use of the cardinal ligaments, the pubocervical fascia, the uterosacral ligaments and the upper portions of the broad ligaments as a supporting structure to uphold the vaginal vault and the bladder. The other is the Manchester operation, with or without modification. This usually employs the bases of the broad ligaments and the pubocervical fascia as means of support, the cervix being nearly always shortened by amputation. Advancement of the bladder is essential in this operation. Use of the round ligaments to hold up the stump of the uterus after subtotal hysterectomy, has long since been found ineffectual, as has the attachment of the cervical stump or uterine fundus to the anterior abdominal wall.

Vaginal surgery requires a definite knowledge of the anatomy of the region and familiarity with the technique of operations done in this field. Results from operations for descensus done from below are much better than following abdominal procedures. Also the safety of this type of operation is greater.

In about 600 vaginal hysterectomies the operation was done for descensus of varying degree in 160 cases. In many of these, with extensive descensus, an unhealthy cervix was found. Occasionally small fibroids were present.

The author gives in detail a description of the technique employed in the cases he observed. When the uterus, or a large part of it, had escaped from the vagina, the Mayo operation was used. This procedure has been described by Ward and somewhat modified by him. In addition to this method the author has found it of value to use the pubocervical fascia, dissected free early in the operation and brought together over the united broad ligaments. An inverted T-shaped incision is made on the anterior wall extending nearly to the urethra. Flaps are freed on each side and the fascial layer dissected free; the flap is important and should be as intact as possible, using a knife for the purpose. The anterior peritoneal fold is opened. Incision is extended around behind the cervix and the posterior peritoneal pouch opened. Uterosacral ligaments caught with short clamps and divided. The uterus is turned out anteriorly, the broad ligaments caught in three clamps on either side and the uterus removed. The uterosacral ligaments are then approximated. Where there is a marked enterocele it is well to resect a portion of the uterosacral pouch. Efficient closure of the posterior part of the weakened uterine supports is most important. Whether part of the

pouch is removed or not, the uterosacrals are united with three or four transverse sutures. The broad ligaments are closed with a running mattress suture passed back of the clamps, which are removed in succession from below upward as the suture proceeds. The suture is locked at the top, and then as a running suture is brought back to the place of beginning. The anterior edge of the sutured ligaments is fastened below the rami of the pubes, and as close to them as possible, by a stitch on either side. This closes the anterior gap and prevents the bladder from escaping forward. If a gap remains between the uterosacrals and the hammock of broad ligaments it is sutured. A firm floor has been formed on which the bladder rests. Over this is sutured the pubocervical fascia and the mucosa closed, after removing the excess, No. 0 chromic gut being used. A perineal repair is then carried out. It is essential to distinguish between enterocele and rectocele.

A change is made in the procedure when the uterus cannot be brought entirely out of the vagina, as it is then not easy to use the running mattress suture. The broad ligaments are caught in clamps, three on each side, ligated and divided, and the uterus brought out either anteriorly or posteriorly. The ligated ligaments are united in the median line and the pubocervical fascia brought together over them. Closure of the uterosacral ligaments is done as described.

Experience has shown that closure of the posterior hernia which comes down through the interval between the uterosacral ligaments is extremely important, preventing recurrence of the enterocele.

Removal of the uterus is particularly useful when the descensus is marked. Operations of the Manchester type are used by the author as a rule in cases where the descensus is not too marked, or when the patient has already undergone subtotal hysterectomy and the cervix has subsequently come down. It may also be used when a previous laparotomy renders hysterectomy difficult.

In cases of marked descensus the uterus is often unhealthy. With the Manchester type operation little is left of the uterus after amputating a sufficient length of cervix.

A persistent rectouterine pouch of the fetal type may predispose to descensus, and this congenital condition may be responsible, in many nonparous women, for descensus of the uterus.

In cases in which incontinence was a symptom, the Kelly procedure was generally used in an attempt at correction. It is easily combined with the anterior colpoplasty.

In the series of over 600 vaginal hysterectomies done for all causes, only one death occurred, a mortality rate of 0.16 per cent. The operation in the more advanced cases of descensus is almost extraperitoneal, and is withstood very well by women of even advanced years. In 12.5 per cent of the author's cases, or 20 in number, the result was not altogether satisfactory. In 87.5 per cent the result was satisfactory. This means a good anatomic result—a flat and well supported anterior wall, a complete cure of enterocele, and a well-healed perineum.

Following the operation a vaginal pack is inserted for twenty-four hours; it is

less for hemostasis than for support. The bladder is emptied by catheter while the patient is still on the table, and further catheterization carried out as necessary.

Convalescence is usually uneventful. In the series 53.3 per cent had fever two or more days, the extensive dissection giving rise to some absorption.

Six figures. Discussion.

(Danforth, perhaps next to Heaney, has been the leading champion of vaginal hysterectomy in this country, and has done much to popularize the technique. Aside from vaginal hysterectomy in general as compared with the abdominal route, there can be no doubt as to the efficacy of the operation, as described by him, in the management of cases of the groups which he details in his paper. Gynecologists will differ as to the choice between vaginal hysterectomy and operations of the Manchester type in individual cases. Certainly vaginal hysterectomy is preferable in the more extreme cases of prolapse, associated with extreme elongation and atony of the ligaments. That the author himself recognizes the wisdom of individualization is evident, since he explains that he prefers operations of the Manchester type in the more moderate degrees of descensus.

The technique as described by Danforth is essentially that which is generally employed, although each operator is apt to add certain individual touches, often of no vital importance. Certain extremely important technical points, however, are forcefully emphasized. For example, the importance of closing the suburethral space is perhaps not as generally recognized as it should be. No matter how good an operation is done otherwise, prolapse of the urethra and bladder neck will often occur through this space if it is not closed off. Even more important is obliteration of the cul-de-sac, by firm approximation or purse-string plication of the uterosacral ligaments. In spite of the greatest care in this respect, pelvic enterocele may at times occur, and as a matter of fact, this is, in my experience, the chief late hazard of vaginal hysterectomy.

In general the vaginal route of operation has probably not been as popular as it should be, although, on the other hand, I have often seen it employed, as for example in vaginal hysterectomy for large myomatous uteri requiring morcellation, when abdominal hysterectomy would have been very much easier. In such cases the vaginal operation seemed a surgical stunt rather than a judiciously selected procedure. On the other hand, one must suspect that the unreasoning opposition to the vaginal route manifested by some gynecologists and most general surgeons may be due to the fact that they have not thoroughly trained themselves in the anatomy of this region and the technique of operations in this field.

Certainly no one will in this day disagree with Danforth's statement that operations for descensus should be done from below and not from above. A prolapsed organ must be supported from below and not hung from above. The practical point of the whole discussion is that the well-trained gynecologist will have at his disposal the anatomic knowledge and the techniques required for both the abdominal and vaginal routes, and that he will select the route which in his judgment best fits the indications of the individual case.—Ed.)

## STUDIES CONCERNING MORBIDITY AND MORTALITY FOLLOWING HYSTERECTOMY

JOSEPH H. PHILLIPS

Am. J. Obst. & Gynec., 50: 174-179, 1945

The series on which this study is based included 643 complete, 253 subtotal and 84 vaginal hysterectomies done over a two-year period in a gynecological

clinic. These figures include both private and ward, and white and Negro patients. Leiomyoma was the most frequent indication for operation, being encountered in 472 (48.1 per cent) of the cases. Postoperative complications were present in 9.9 per cent of the complete, 11 per cent of the subtotal, and 53.1 per cent of the vaginal hysterectomies. The most common causes of morbidity were: femoral phlebitis (1.8 per cent of complete and 1.1 per cent of supravaginal hysterectomies); cystitis (1.4 per cent of complete, 1.5 of supravaginal, and 2.3 per cent of vaginal operations); abdominal wound sepsis (1.2 per cent of complete and 2.7 per cent of supravaginal operations); pelvic peritonitis (0.9 per cent, 2.7, and 45.2 per cent, respectively, by type of hysterectomy); and postoperative vaginal hemorrhage (0.7 per cent of complete and 2.3 of vaginal operations). Morbidity manifested by elevated temperature and pulse rate of unknown cause occurred in 19.8 per cent of the complete and 20.9 per cent of the supravaginal hysterectomies. Deep femoral phlebitis occurred only in patients over 35 years of age. Operations on patients with benign chronic pathological conditions were followed by a low incidence of morbidity, but patients with malignant growths of the uterus or the adnexa suffered from frequent complications. There were four deaths in the entire series, and two of these were in patients over 65 years of age, with adenocarcinoma of the endometrium. No deaths occurred in the subtotal hysterectomy group. It is thought that the high morbidity and mortality rates in the vaginal hysterectomy group were due to the extensive plastic procedures and opening of the peritoneum which routinely accompanied the operation. All of these patients had procidentia with cystocele, rectocele, and enterocele. The average age of these patients was higher (53.9 years) than that of the complete (43.6 years) and subtotal (40.7 years) hysterectomy patients.

(The figures given by the author as to the proportionate distribution in this series of complete, subtotal and vaginal hysterectomies are of interest. They may be taken, first of all, as indicating that the preference of this clinic is for the total operation over the subtotal operation, and that the latter is probably performed unless there is some definite contra-indication, technical or otherwise. This is in keeping with the attitude held by most gynecologists of today, and the long drawn out controversy over total vs. subtotal hysterectomy appears to be drawing to a close.

Furthermore, the figures as well as the statements of the author, indicate that vaginal hysterectomy is done only in those cases in which the hysterectomy is to be combined with correction of procidentia and cystocele, rectocele and enterocele. This is likewise in keeping with the practice of most American clinics, although a lusty minority prefer the vaginal route for most cases of intrinsic benign uterine pathology, regardless of any associated indication for plastic procedures.

It is difficult to explain the high morbidity after the vaginal operation, in spite of the factors suggested by the author, and it would seem out of line with the common experience along this line. Especially surprising is the reported incidence of pelvic peritonitis in 45.2 per cent of the vaginal group. The paper deals only with morbidity and mortality, not including later follow-up study of such late complications as for example, pelvic enterocele after vaginal hysterectomy. See also comment on preceding abstract of paper by Danforth. —Ed.)

LACERATIONS OF THE PERINEUM AND THEIR REPAIR. A STUDY  
BASED ON 2328 PERSONAL CASES

LOUIS E. PHANEUF

Surg., Gynec. &amp; Obst., 81: 320-326, 1945

As the author has previously published his technique of the operation for complete tears of the perineum, this paper is limited to a description of his technique of performing late or secondary perineorrhaphy for incomplete tears. The success of this operation depends on careful preparation of the operative field and maintenance of a rigid asepsis; sharp rather than blunt dissection whenever feasible, to avoid bruising the tissues; the approximation of the tissues in layers (preferably four) rather than mass approximation, since this maintains suppleness and elasticity, as well as support, and avoids painful rigidity; employment of fine suture material and accurate approximation of the tissues without tension; and carefully planned and executed postoperative care. The details of the procedure are as follows:

Two nights before entering the hospital, the patient takes a saline cathartic, and, after the bowels have been thoroughly evacuated, remains on a light diet until admission. The afternoon before operation the external genitals are shaved and gently scrubbed with gauze and tincture of green soap, particular attention being paid to the anus, to the folds about the vulva, and to the mons veneris. The parts are then rinsed with nonirritating potassium mercuric iodide solution, 1:1000. A vaginal douche is given, consisting of two drachms of compound zinc sulfate powder in two quarts of warm water. A soapsuds enema is administered the afternoon or evening before operation. After induction of anesthesia the parts are prepared in the operating room by cleaning the external genitals with ether and painting them with tincture of zephiran and by painting the vagina with tincture of zephiran. In the presence of considerable vaginal discharge, the vulva and vagina are gently scrubbed with tincture of green soap and warm water, rinsed with 1:1000 potassium mercuric iodide solution, and painted with tincture of zephiran. Sterile drapings are applied, and the anus is covered with a sterile gauze sponge which is held in place by means of two towel clips.

To spread the labia apart Friedman or Gelpi retractors or fine silk sutures held in hemostats on each side of the vulva and at the posterior commissure may be used. The pelvic floor is opened at the mucocutaneous border by means of Emmet scissors, Mayo scissors, or a scalpel. The posterior margin of the incision is held in the median line with an Allis forceps, and posterior vaginal wall is separated from the rectum and the perineal muscles by sharp and blunt dissection, using the gauze covered fingers. The separation of the posterior vaginal wall from the rectum and the perineal muscles is facilitated by using a T forceps, which holds the vaginal wall firmly and does not slip. The perineum is then reconstructed by approximating four layers of tissue. The crura of the pubococcygei muscles are approximated in the median line by three in-

interrupted sutures of No. 0 chromic catgut, to narrow the space between the anteromedial margins of the levator ani muscles and to overcome the rectocele. The second layer comprises the urogenital diaphragm, made up of the deep transversus perinei muscle and its covering fasciae. Three sutures of the same material are placed in these structures and left untied. A triangle of the posterior vaginal wall with the apex at the crest of the rectocele is resected. When there is considerable redundancy, this is facilitated by the use of Ochsner clamps on each side, but they may be omitted if the opposite condition exists. The vaginal part of the incision is closed with interrupted sutures of No. 0 chromic catgut and the three sutures in the urogenital diaphragm are tied and cut. The skin edge is freed from the underlying scar tissue so that it can be approximated later without tension. The third layer, consisting of Colles' fascia, is united with a continuous suture of No. 00 chromic catgut. The skin forms the fourth layer and is approximated with a running suture of No. 00 chromic catgut, the ends of which are arrested with lead shots. At the lower angle of the skin incision, there is always redundant tissue, which, if not removed, appears as a protuberance. It is important to resect this tissue in order to leave a flat surface when the suture is completed. At the completion of the operation the only part that shows is the 2.5 to 5.0 centimeters of skin which covers the operative field. By using lead shots instead of tying the sutures and resecting the skin at the lower angle of the incision a flat, even surface with a satisfactory plastic result is obtained. The vagina is loosely packed with iodoform gauze, the end of which is held by a silk suture attached to the inner aspect of the thigh by a small piece of adhesive plaster to facilitate the finding of the gauze for removal 24 hours later.

Morphine and codeine are prescribed to allay pain. The suture line is painted with 4 per cent mercurochrome or aqueous solution of zephiran after each micturition and defecation. Forty-eight hours after operation a douche of one drachm of compound zinc sulfate powder in one quart of warm sterile water is given and repeated daily until the patient leaves the hospital. If catheterization is necessary in the first few days after operation great care should be used in separating the labia to expose the urinary meatus, since the upper part of the incision is held by fine catgut sutures and may separate if force is used. The bowels are moved on the third postoperative day. A fairly generous diet is given on the fifth postoperative day. The patient is allowed out of bed on the morning of the twelfth day, and is discharged from the hospital on the fourteenth day.

A brief review is given of 1,556 gynecologic or secondary operations on the perineum and 772 obstetric or primary operations performed by the author. The first group were classified as follows: perineorrhaphy for incomplete laceration, 1,448 cases; perineorrhaphy for complete laceration, 101 cases; plastic operation to enlarge the vaginal introitus, 6 cases; excision of the sinus of the perineum, 1 case. In the total group there were 12 deaths. The details of these deaths are given in case summaries. In all of them perineorrhaphy was done as a complement of an extensive gynecologic operation and the deaths were due to the disease for which the main operations were performed rather than to

the perineorrhaphy. The obstetric repairs were classified as: episiotomy, 396 cases; repair of lacerations varying from a small tear in the mucosa to a second degree tear, 367 cases; repair of third degree tear, 9 cases. The two deaths in this group were attributed to causes other than the operation.

(The details of the procedure carried out by Phaneuf emphasize the meticulous and painstaking care which he puts into his plastic surgery, and which explain the excellent results which he obtains. The slap-dash type of operator cannot expect to match these results. Gynecologists will always differ as to the details of operation, and each is likely to have his individual tricks and touches. There is more opportunity for individualization in vaginal than in abdominal surgery, where there is a greater approach to standardization of techniques. Generally speaking, I have always felt that one can arrive at a better evaluation of a gynecologist's caliber by watching him perform a not too simple vaginal plastic operation than by seeing him do, for example, a simple hysterectomy.—Ed.)

## HEMINECROSIS OF CERVICAL STUMP FOLLOWING SUPRAVAGINAL HYSTERECTOMY

ROBERT T. FRANK

*Am. J. Obst. & Gynec.*, 50: 226-227, 1945

This is a case report. The patient, a 39-year-old nullipara, had been aware of the presence of uterine fibroids for seven years. The uterus was enlarged and distorted by multiple myomas which were mainly retrocervical. A supravaginal hysterectomy for fibroids, right salpingo-oophorectomy for closed hemato-salpinx and appendectomy were performed. Both ligatures to the uterine arteries were applied at the same level. Postoperative convalescence was smooth and afebrile until the tenth day, when slight bleeding from the vagina was noted. On the eleventh day, the bleeding became profuse, the temperature rose to 103.6° F, and white blood counts of 19,000 and polynuclear counts of 60 per cent developed. Sulfadiazine by mouth was prescribed. Speculum examination revealed a sharply demarcated necrosis of the right side of the cervix extending into the right fornix. Three days later the entire necrotic area was removed as a slough. A raw depression in the lateral fornix close to the course of the right ureter and uterine artery was exposed, and packing of iodoform gauze was inserted against it. No secondary hemorrhage developed and the patient was discharged fully healed on the twenty-sixth day. Complete cicatrization was observed six months later. It is assumed that the vaginal vessels on the right side were anomalous and did not possess the customary free anastomosis with the ascending vaginal vessels, and that consequently the affected area became ischemic and sloughed off. If the process had been due to thrombosis and infection, further extension into the fornix with secondary hemorrhage from the uterine artery might have occurred.

(This is certainly an unusual and perhaps unique complication of supravaginal hysterectomy, and it is difficult to explain the mechanism involved, in view of the free anastomosis

between the uterine and cervical arterics with the vaginal vessels of the two sides. The explanation suggested by the author of a circulatory anomaly of some sort appears to be as plausible as any.—Ed.)

## A METHOD FOR THE SURGICAL OBSTRUCTION OF THE FALLOPIAN TUBE. ANIMAL EXPERIMENTATION

EARL GEORGE KRIEG

Surg., Gynec., and Obst., 81: 331-334, 1945

In the literature on the subject of surgical obstruction of the Fallopian tube a variable number of failures due to re-establishment of a communication between the abdominal and uterine cavities have been reported. The present investigation was undertaken primarily to test a modification of the Madlener technique designed to eliminate the failure of closing the passage completely. During this study several probable causes of failure in the original technique were found and are reported in this paper.

The experiments were carried out on the cornua of medium sized bitches. In some experiments the cornua were crushed by forceps in 2 areas and then tied; in others the segments were tied tightly without preliminary crushing. In two experiments an additional crushing, with a suture placed distal to the standard procedure, was done for comparison. The lumina of the segments thus produced were injected with sclerosing solutions. Longitudinal sections were studied.

It was found that adequate trauma must involve the mucous membrane layer in order to produce stenosis of the cornua in the dog. The degree of physical trauma was difficult to gauge when induced by crushing without the addition of chemical trauma. Carnoy's solution and 75 per cent phenol solution produced the most extensive changes; quinine hydrochloride and urethane and sodium morrhuate solutions produced only mild reaction and were considered inadequate.

Simple tying without preliminary crushing did not traumatize the mucosa sufficiently and in such experiments a patent lumen was re-established. Other causes of failure suggested by the study include: (a) Absorbable suture does not remain in place a sufficient length of time; (b) Rapid crushing may cause shearing of the wall with resultant fistula formation; (c) Heavy cornual musculature which is present during pregnancy or estrus may lead to incomplete crushing. Cystic areas of hydrosalpinx in the segments between the sutures or above them were produced in several dogs which passed through a period of estrus during the conduct of this study.

## STERILITY

### A SIMPLE TECHNIQUE TO TEST TUBAL PATENCY

ALBERT DECKER

Am. J. Obst. & Gynec., 50: 227-229, 1945

A description is given of a method of production of pneumoperitoneum by the transuterine route, which is much simpler than Rubin's technique and can be carried out in the physicians's office with instruments at hand. The patient is placed in the knee-chest posture and the perineum is elevated with a Sims speculum. The cervix is exposed, painted with merthiolate, grasped with a tenaculum, and an intrauterine cannula or metal catheter is introduced into the uterus. The negative intra-abdominal pressure causes immediate pneumoperitoneum if the tubes are patent. The amount of air entering the abdomen can be demonstrated by x-ray or fluoroscope, and amounts usually to about 150 to 300 cc. The negative pressure created in the abdomen by the knee-chest posture, attains 8 to 12 cc. of water, as measured by the Zavad Aneroid Pneumo apparatus. The characteristic shoulder pain and symptoms of pneumoperitoneum occur on resumption of the sitting or standing posture. Pneumoperitoneum can also be produced after slight dilatation of the cervix with a cervical dilator and without introduction of a cannula. Advantages of the technique are as follows: the air enters the abdomen only if the tubes are patent, not spastic; the pressure within the uterine cavity is never elevated; the danger of air embolism is reduced; accidents resulting from high intrauterine and intratubal pressure are avoided; and a positive result will make other procedures unnecessary. It does not offer the diagnostic details that can be obtained by more elaborate apparatus nor is it a therapeutic measure to overcome obstruction of the oviduct. A case history is presented to illustrate the results obtained by this technique.

(While the method described is simple enough, it is scarcely more so than the universally employed tubal insufflation technique of Rubin. It has the disadvantage of admitting air to the abdominal cavity rather than the much more quickly absorbed carbon dioxide used in the Rubin test, which is quite reliable without x-ray check. Much more important, the author's plan lacks the quantitative information yielded by the Rubin method as to degrees of pressure and tubal peristaltic tubal activity. It can therefore hardly be expected to compete with the latter in usefulness or applicability.—Ed.)

## RESULT OF INTRA-UTERINE LIPIODOL INJECTION: CASE REPORT

J. D. FLEW

Proc. Roy. Soc. Med. (Sect. Obst. &amp; Gyn.), 37: 425, June, 1944

In the belief that more might be learned if our failures, rather than our successes, were more frequently discussed, the author makes the following report of the result of an intra-uterine lipiodol injection performed in the routine investigation of a case of sterility.

The radiograph showed a "fluffy" appearance around the body of the uterus; and loops of lipiodol were obvious in the broad ligaments extending upwards in the region of the ovarian vessels.

When the author observed this in the wet film, he kept the patient in bed; but twenty-four hours later she developed acute pain in the chest followed by a small hemoptysis. During this time she also had severe constant headache, and, three days after the injection, was found to have a left hemiplegia.

Unfortunately no portable X-ray was available, but there seems but little doubt that she had a lipiodol infarction of the lung, and cerebral embolus. Fortunately both these complications cleared up without further extension. She did, however, develop a severe pelvic cellulitis, which kept her in bed for six weeks.

The mistake in this case, performed eight years ago, lay in the fact that the lipiodol injection was carried out some three to four days before the patient's period was expected instead of in the postmenstrual phase, and, as a result, the congested endometrium was eroded by the canula and the lipiodol injected into the blood-stream.

(While both of the commonly employed tubal patency tests, insufflation and hysterosalpingography, are ordinarily safe procedures, accidents are possible with either. A small group of cases of gas embolism following tubal insufflation have been reported, though almost always when air has been employed instead of the far better and safer carbon dioxide. In the same way intrauterine oil injections are not free of all danger, especially when there are flaws in technique, as the above case will illustrate.—Ed.)

## SOME RECENT STUDIES AND INVESTIGATIONS IN STERILITY

ALBERT SHARMAN

Proc. Roy. Soc. Med. (Sect. Obst. &amp; Gyn.), 37: 67-72, (December, 1943)

This communication deals with certain aspects of sterility as follows: (1) the estimation of tubal patency; (2) anovular menstruation as assessed by endometrial biopsy; (3) endometrial tuberculosis; and (4) the causation of tubal occlusion.

*Tubal patency.* The total number of patients in the series whose tubes were insufflated, amounted to 480, of whom 232 had two or more insufflations. In most instances the test was repeated as a confirmatory procedure. In twenty-two patients six or more insufflations were done to study the behavior of the tubes over a considerable period of time. These repeated insufflations have shown that a single finding of non-patency is not reliable. In twenty-five of the author's patients the initial insufflation indicated that the tubes were closed but subsequent insufflations showed that they were actually open. None of these patients, however, showed non-patency on insufflation on more than one occasion. Moreover, in a series of 60 cases studied first by insufflation and later by lipiodol injections, the latter procedure showed that insufflation had erroneously indicated blockage in 6 cases. Among 115 patients who became pregnant later, 29 had been diagnosed as having non-patent tubes as a result of a single insufflation. It has been suggested that a finding of patency subsequent to one of non-patency may be explained by the therapeutic effect of the first test. This view finds no substantiation in the author's results since if non-patency were found on two or two or more occasions, no success in restoring patency was achieved by repeated insufflation.

The practical conclusions which the author draws from his insufflation series are: (1) In cases of tubal patency, an isolated or occasional finding of apparent patency may occur and this, equally in anesthetized and non-anesthetized subjects, and (2) The result of a single insufflation with or without anesthesia showing apparent non-patency cannot be depended upon.

In an effort to find the cause of this "pseudo-blockage" the author studied (1) the effect of anesthesia; (2) the time-relationship of insufflation to the phase of the cycle, particularly the premenstruum; and (3) the rate of flow of the gas. The results were negative in that none of these factors proved to be a cause of the "pseudo-blockage."

In the author's series hysterosalpingography was chiefly done for comparison with insufflation. There is little to be added to the findings of previous workers in this field. His own observations have led to this conclusion: If each test is performed once only, the percentage of error is about equal, namely 10%. In all but 6 of 60 cases where lipiodol showed patency, tubal insufflation also did; and in all but 4 of 40 cases where lipiodol showed non-patency, tubal insufflation also showed non-patency. But the error in tubal insufflation is reliance on a single test, which error can be avoided by repeating the test, whereas the error in hysterosalpingography is in the reading of the plates and is not always remediable.

*Anovular menstruation.* Endometrium was removed in 358 cases in the premenstrual phase of the cycle, in over 80% of instances by means of a biopsy curette in the non-anesthetized patient. Of these, 335 showed the normal, characteristic, secretory features of this phase; 23, i.e. 6.4%, showed anovulatory cycles, 11 of these on one or more occasion but not on all, and 12 on all occasions on which biopsy was performed. The author emphasizes that an erroneous diagnosis of anovular cycles may be made if reliance is wholly placed

on the date of the preceding menstruation and biopsy is performed only in the presumptive premenstrual phase. The date of menstruation after biopsy must be ascertained.

*Endometrial tuberculosis.* The examination of endometrium in 392 of the original series of 500 cases showed unsuspected tuberculosis in 20, i.e. 5.1%. Since the completion of that series a further 448 consecutive and unselected cases of primary sterility have had endometrium examined and of these 22 have shown tuberculosis, i.e. 4.9%. This gives a total incidence of 5% in 840 cases. The author cites evidence moreover to show that this figure of 5% in his series is an absolutely minimal one. Endometrial tuberculosis was found to be still in evidence after lengthy periods of time in 6 patients, that is after several years. Follow-up, moreover, showed that not one sterility patient with endometrial tuberculosis became pregnant. Reinfection of the endometrium recurred rapidly after curettage. In 35 cases of endometrial tuberculosis in which insufflation was carried out 29 showed tubal blockage, an incidence of 83%. This extremely high incidence of occlusion suggested the possibility of an unsuspected sub-clinical tuberculous salpingitis as the source of infection of the endometrium.

*Causation of tubal occlusion.* The author limits his discussion to the etiology of blockage in tubes which appear normal on bimanual examination. He cites evidence to show that the gonococcus is seldom responsible for the occlusion of tubes which are not palpably thickened. Nor in his opinion is congenital hypoplasia a cause of tubal occlusion since he was able to demonstrate that the fallopian tube in the prepubertal state, indeed, in infants and fetuses, is patent both histologically and as shown by insufflation. The author then returns to his previously mentioned findings in respect to endometrial and tubal tuberculosis and reaches the conclusion that a considerable number of cases of tubal blockage are the result of a subclinical tuberculous salpingitis.

(This excellent paper should be read by everyone interested in the study of sterility. With reference to tubal patency tests, the author very properly emphasizes that no woman should be convicted of tubal non-patency on the basis of a single insufflation test, the possibility of error on the first test being about 10 per cent. The same proportion of fallibility pertains to hysterosalpingography, which the author says he employed chiefly for comparison with insufflation. Reading between the lines, one gets the impression that he prefers insufflation for the routine study of tubal patency, and this will probably be the feeling of most gynecologists.)

On the other hand, in some of our own clinics, there is much enthusiasm for hysterosalpingography, which is made a part of the routine in the study of sterility cases. Certainly there can be no doubt as to the greater simplicity and inexpensiveness of the Rubin technique, and I know of no convincing evidence indicating any advantage of hysterosalpingography in so far as accuracy and possible therapeutic value are concerned. Its one clear advantage is in locating the site of tubal obstruction. This is of little practical advantage to the patient unless plastic operation is contemplated. Even then it is not indispensable, as the reverse insufflation so readily done at operation is of even more precise value in locating the seat of tubal block. For that matter, every gynecologist who has done any number of such operations has had the experience, often rather mystifying, of finding the tubes patent on reverse insufflation when perhaps repeated pre-operative tests had indicated their non-patency. There are many other angles of this question, but it is probably

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Where the ovarian changes occurred early in life, uterine hypoplasia was usually found. With secondary amenorrhea, however, the uterus was of normal size, except when the amenorrhea had persisted two to eight years. In these cases the uterus had diminished in size and even atrophied.

Hirsutism was present in fully 50 per cent of patients, being particularly noted in adolescent patients. Secondary sex characteristics are of two types, the true feminine, and those with masculinizing effects, the former exhibiting no abnormal hair distribution.

Breast development varied, with no apparent relationship between this and hirsutism. In a case of primary amenorrhea there was practically no breast development,—merely a papule-like elevation. After surgical treatment of the ovaries rapid development took place in a few months, and after the birth of a child the patient was able to nurse the infant.

Obesity was present in about 10 per cent of the patients in the series, but as the basal metabolic rate was within normal range, it seems no more common than in other gynecologic conditions.

Polycystic ovaries are often not recognized on routine pelvic examination, being difficult to palpate; also because more than one-third of the patients are single and recto-abdominal palpation is not conclusive. Because of the various difficulties encountered in diagnosis by palpation, gynecography was utilized. In every instance where this method was employed and polycystic ovaries found on films, the diagnosis was corroborated at operation.

In the present study, surgical treatment in the form of bilateral ovarian wedge resection and suture of the ovaries was carried out in 53 patients. This proved to be a satisfactory and most successful method of therapy. Seventeen married patients and three of the single patients who subsequently married, became pregnant after operation, resulting in 26 pregnancies and 28 babies. Periodic check-up postoperatively revealed that there were no recurrences of polycystic ovaries, although three single women who had febrile and painful postoperative courses, developed a unilateral ovarian cyst with adhesions. On the basis of his study, the author recommends that bilateral polycystic ovaries, associated with amenorrhea, sterility and/or hirsutism, be treated by bilateral ovarian wedge resection.

(Stein has published a number of papers on this subject over the years, although the operation which he advocates does not appear to have received any wide acceptance, to judge from the paucity of reports from others. From the description he gives of his "syndrome," it would appear to be a variant of the so-called hypopituitary cases. In many cases of pituitary dysfunction, hirsutism is noted, in others not. When present it is believed by many to be due to adrenal participation in the disorder, and it is not easy to delimit the pituitary and adrenal rôles. The best illustration of this is seen in the fact that an identical Cushing syndrome can be produced by either an adrenal adenoma or by a basophilic adenoma of the anterior lobe.

While claiming good results from resection of the ovaries in cases of the type he describes, Stein has always honestly admitted his inability to explain them. A possible factor might be that, according to the Lipschütz "law of follicular constancy," the reduction of ovarian substance makes for a greater concentration of gonadotrophic effect upon the residual ovarian tissue. The same mechanism perhaps explains the frequent enlargement and

quite evident that, with full appreciation of the fact that there is a place for both methods, my personal preference is for tubal insufflation for routine use.

The author finds 6.4 per cent of anovulatory cycles in his series of cases, which is within the extremes of the widely differing figures reported by various observers. There is little doubt that the age groups in different series have some bearing on such observations. In women over 35 it is quite certain that the proportion of anovulatory cycles would be higher than in younger patients. Sharman very wisely emphasizes the possibility of erroneous diagnosis of anovulatory cycles unless the date of the succeeding menstrual period is checked. To obviate this possibility, and also to minimize the possibility of disturbing a possible unsuspected early pregnancy, it is better, when feasible, to defer the biopsy until the menstrual period has actually begun. The necessary histological information can be obtained within many hours of the onset, though the earlier in the bleeding phase the better.

Perhaps the most interesting and most startling section of Sharman's paper is that based on his finding of unsuspected tuberculosis in the endometrium of 42 of 840 cases, an incidence of 5 per cent. While most gynecologists can testify from personal experience that occasional instances of endometrial tuberculosis are revealed by biopsy for sterility investigation, there are probably few who would put the proportion as high as Sharman has reported. Since the presence of endometrial tuberculosis practically presupposes tubal tuberculosis, it is not surprising that Sharman's follow-up showed that not a single patient with endometrial tuberculosis became pregnant, and that 83 per cent of these patients showed non-patency of the tubes on insufflation. The practical point to be derived from Sharman's results is that perhaps we should aim to get more tissue with our biopsies than is feasible with some of the instruments and techniques so commonly employed in this country. It is just as easy, with proper methods, to get abundant tissue, or for that matter, to do a fairly complete curettage. Nor would there seem to be any disadvantage to this, since neither anesthesia nor hospitalization is ordinarily required.—Ed.)

## BILATERAL POLYCYSTIC OVARIES. SIGNIFICANCE IN STERILITY

IRVING F. STEIN

*Am. J. Obst. & Gynec.*, 50: 385-98, October, 1945

Bilateral polycystic ovaries are associated with a definite syndrome, the characteristics of which are menstrual irregularity, featuring amenorrhea, sterility, hirsutism, sometimes retarded breast development and obesity. In addition there is in some cases extreme masculinization and facial acne. Occasionally there is pelvic pain. In diagnosing this condition pneumoroentgenography is of great value. Surgical treatment is necessary.

The author states that fifteen years ago the first wedge resection was done for bilateral polycystic ovaries, for relief of amenorrhea and sterility. This is the third five year report on the subject. He emphasizes the importance of the syndrome in the study of sterility. This disease of the ovaries is not congenital, inflammatory or degenerative, but the result of an endocrine disturbance. Amenorrhea of varying degree is a conspicuous feature of the course of these patients, some never menstruating; but the largest group having irregular periods. In rare instances normal sex cycles began at puberty and continued for some years; even a pregnancy occurred before the cyclic disturbances appeared.

## ANAEROBIC METABOLISM OF SPERMATOOZOA

T. MANN

Nature, 156: 80-81, 1945

It is known that the presence of oxygen is not essential for the survival of spermatozoa and that they retain their motility under anaerobic conditions provided that glucose is present. It has also been demonstrated that the metabolism of spermatozoa is predominately glycolytic in character. Heretofore, however, studies have been largely confined to the investigations of normal conditions, various substrates and inhibitors of sperm glycolysis, leaving open the question concerning the glycolytic pathways and the enzymes involved in the anaerobic processes. The presence in sperm of adenosinetic phosphate, one of the essential factors of glycolysis, has been assumed on the grounds that the sperm contains a phosphate fraction which breaks down to orthophosphate after short hydropysis in acid.

Metabolic studies on ram semen were carried out by the author with several notable findings. Spermatozoa do contain adenosinetic phosphate which was isolated quantitatively in the form of the barium salt. When spermatozoa are incubated anaerobically without glucose, their content of adenosinetic phosphate decreases rapidly, while in the presence of glucose it can be preserved much longer. This behavior is in agreement with the observation that in spermatozoa stored anaerobically motility is maintained more satisfactorily in the presence than in the absence of a glycolysable substrate. The metabolism of glucose in the sperm is initiated by the shift of the labile phosphate groups from adenosinetic phosphate to glucose. The enzyme which catalyses this reaction resembles the hexokinase of yeast.

In sum, two major points emerge from the author's investigation. First, the fact is established that a close relationship exists between the activity of the spermatozoa on one hand, and the glycolysis mediated by adenosinetic phosphate on the other. Secondly, it is shown that the glycolytic pathways and enzymes involved in the anaerobic metabolism of spermatozoa bear resemblance to those of other animal tissues and yeast.

## PRESERVATION OF HUMAN SPERMATOOZOA AT LOW TEMPERATURES

A. S. PARKES

Brit. Med. J., 2: 212-213, 1945

The experiments described in this paper were undertaken in an effort to explain some of the discrepancies in results found in the literature on the low-

"cystic" changes occurring when only a portion of one ovary has been conserved at operation.—Ed.)

## MEETING ON SEMINOLOGY

ARRANGED BY FAMILY PLANNING ASSOCIATION, CAMBRIDGE

Brit. Med. J., 2: 230, 1945

Brief reports are given of two papers presented at the meeting.

Dr. Margaret Hadley Jackson discussed the post-coital test for semen analysis, including examination of the vaginal pool and cervical mucus, as done at the Exeter Family Planning Association Clinic. Between 600 and 700 tests had been done on most days in the cycle, and at times after coitus varying from half an hour to 12 days in both fertile and infertile wives. It was usually possible to find sperm, if the test was repeated often enough within 12 to 15 hours after coitus, even when the husband had a sperm density as low as two or three million per ccm. Even in infertile couples, cases in which early post-coital test remained persistently and completely negative were rare. Evidence was produced which suggested that tests done 40 hours or more after coitus might provide a more valuable measure of adequate fertility.

Data presented by Mrs. Clare Harvey suggested that most abnormal types of human spermatozoa might be produced by degenerative changes in sperms which had been morphologically normal when first detached from the germinal epithelium, and that morphologically abnormal spermatozoa were aged spermatozoa. Most specimens produced a week or more after the previous ejaculation showed a higher abnormal count than those produced at shorter intervals. It was suggested that the average age of spermatozoa at ejaculation might be increased by delay in the journey from the testis through the epididymis and vas. There appears to be a close relationship between the motility of the spermatozoa and their age. Data from 130 semen analyses showed that in at least 75 per cent a high motility and good morphology, or a low motility and poor morphology, were combined.

(Dr. Jackson's suggestion that tests be done 40 or more hours after coitus would seem to put the spermatozoa to a pretty rigid test, though it is well known that the organisms can often be found many hours after coitus, much later than the Hühner test is ordinarily performed. An important influencing factor in this regard is the phase of the cycle in which such tests are performed. For example, positive results are most likely to be found at the ovulation phase, when the cervical secretion is apparently freer but more readily penetrable to the sperm.)

Mrs. Harvey's suggestion that morphologically abnormal spermatozoa are aged organisms is of interest, but will need confirmation. The usual concept is that the abnormal types are as a rule to be interpreted as immature forms, and this view is supported by the morphological resemblance of such abnormal organisms to immature cells found in the testis itself.—Ed.)

## MISCELLANEOUS

### RESULTS OF GONOCOCCUS CULTIVATION FROM A GYNECOLOGICAL PATIENT MATERIAL

JENS L. HANSEN

Acta Obst. & Gynec., 25: 18-31, 1945

By means of cultures from urethral and cervical secretions the presence of gonococci was demonstrated in 21 out of 500 female patients in a surgico-gynecological department of a large hospital in Copenhagen. Direct microscopy had revealed the presence of gonococci in only 6 of these patients. Most of the positive cultures were obtained from patients with salpingitis (16 out of 204). In four patients suffering from extragenital affections and presenting no evidence of a genital lesion, the presence of gonococci was disclosed by cultivation.

It is thought that the routine gonococcus cultivation in the surgical departments of the hospitals of Copenhagen annually discloses about 100 otherwise unrecognized sources of gonorrheal infection.

As an additional advantage offered by this method, mention is made of the possibility of the determination of chemoresistance of the gonococci and this may be of some therapeutic value.

Under certain conditions (easy transport, suitable temperature) the cultivation method may be of value in the negative diagnosis of gonorrhea when the outcome of the direct microscopy is doubtful.

The author arrives at the conclusion that in every gynecological examination of patients presenting even the slightest possibility of gonorrheal infection, cultivation for gonococci ought to be performed together with direct microscopy.

(More and more the evidence is accumulating that the decisive diagnosis of gonorrhea must be made by cultures, and these should certainly be resorted to in all doubtful cases.—Ed.)

### SEX DIFFERENCES IN PUBIC HAIR DISTRIBUTION

C. W. DUPERTUIS, W. B. ATKINSON AND H. ELFTMAN

Human Biol., 17: 137-42, May, 1945

Pubic hair distribution has been examined by the authors in photographs of 1060 men and 309 women. The classical division into "masculine" and "feminine" types of distribution is found to be unsatisfactory.

temperature preservation of human spermatozoa. All semen specimens used in the present study were rated normal, were liquified before being used, and were not diluted. No marked differences in resistance to freezing were noted between the various samples. It was found that rate of freezing and thawing is not a primary factor in the survival of human spermatozoa exposed to low temperatures. When minute amounts of semen were frozen as films or in fine capillary tubes spermatozoa did not survive, but when frozen in bulk at  $-196^{\circ}\text{C}$ . or  $-79^{\circ}\text{C}$ . a large proportion survived for long periods. It is at present impossible to determine whether vitrification affects the power of the human spermatozoa to fertilize and activate the ovum and induce normal embryonic development. This question is of great interest. Artificial insemination of human beings will no doubt become increasingly common, and the elaboration of a method permitting of prolonged storage and transport of the semen without affecting the genetic properties of the spermatozoa would open up remarkable possibilities.

(The experiments of Parkes emphasize the now well established fact that spermatozoa are very resistant to cold, resuming their motility and fertilizing potency when thawed out. This fact has long been utilized by stock-breeders and successful animal inseminations carried out with refrigerator semen transported even thousands of miles. Knowledge of these facts is now quite general, so that no longer do gynecologists advise their sterility patients as did those of a former day, to keep warm the specimens of semen brought for examination. As a matter of fact, it is the very body temperature environment into which the spermatozoa enter after injection into the genital canal which is believed to limit their span of fertilizing potency so sharply.—Ed.)

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An adequate classification recognizes four types of pubic hair distribution: (1) horizontal, in which the superior termination of hair growth is in a horizontal line; (2) sagittal, resembling the first except for an additional linear upward extension in the midline; (3) acuminate, having an upward extension triangular in shape and pointing towards the umbilicus; and (4) disperse, in which hair is distributed over the abdomen without forming a discrete geometrical pattern. The first of these types corresponds to the classical "feminine" distribution and the third type to the classical "masculine."

The 1060 men studied were of two age groups; the first was made up of 964 college students averaging 18 years of age and the second consisted of clinical patients ranging in age from 30 to 40 years. Similarly the 309 women comprised 174 college students and 53 clinical subjects. Eighty-two pregnant women formed an additional series.

The acuminate, or "masculine," type of distribution is present in one-half of the men and one-tenth of the women. The horizontal, or "feminine," pattern is the definitive type for nine-tenths of the women. It is also the basic type for male adolescents, is characteristic of 38 per cent of 18-year-old males and persists in 17 per cent of the adult males. Since the horizontal type appears in both sexes at puberty, it would appear that it is the basic pattern from which the other types develop by upward extension. The acuminate pattern is found as frequently in the series of pregnant women as in the other groups of females. Consequently there is no indication of a correlation between fertility and pubic hair pattern.

In males the decrease in frequency of the horizontal pattern with age is associated with an increase in general hirsutism and is accompanied by the development of a disperse pubic hair pattern. A much larger percentage of men with sparse chest hair have a horizontal pattern of pubic hair than those with conspicuous chest hair. Comparably, a much larger percentage of men with sparse hairiness of the thighs exhibit the horizontal pubic pattern than those with conspicuous thigh hairiness.

General hirsutism is consequently an important, but not the only, factor determining pubic hair distribution. The tendency towards general development of hair exhibits itself earlier on the thigh than on the chest. Conspicuous thigh hair is present in 81 per cent of the college men and 77 per cent of the older men, but only 20 per cent of the college men have conspicuous chest hair, compared to 71 per cent in the older group. 4 references.

(This is an interesting statistical study of pubic hair distribution in the two sexes, with no attempt to explain the variations, probably because no one could do this except on very general and very speculative lines, since we know so little as to the interrelationship of the chromosomal and endocrine factors which are involved. The classification of pubic hair types into four groups, as suggested by the authors, seems simple and satisfactory. Certainly the masculine types of pubic hair distribution, when seen in women, or even extreme types of hirsutism are not in themselves evidence of masculinization, for they may be found in women who otherwise are typically feminine from the standpoint of genital development, menstruation, fertility and psychology.—Ed.)

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# *Obstetrics*

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## PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

### THE DAY TO DAY LEVEL OF ESTROGEN AND PROGESTIN THROUGHOUT PREGNANCY AND PSEUDOPREGNANCY IN THE MOUSE

W. B. ATKINSON AND C. W. HOOKER

Anat. Rec., 93: 75-95, 1945

In an attempt to estimate the level of estrogen and progesterone throughout pregnancy and pseudopregnancy in the mouse, the authors observed the histological features induced in the endometrium of the ovariectomized mouse by injection of these hormones.

During pseudopregnancy the structure of the endometrium on the first day indicated low levels of both estrogen and progestin. Thereafter the level of progestin rose progressively for 3 days and remained high through the next 4 days. A decrease in progestin appeared on the ninth day and persisted to reach the initial low level on the twelfth day. The level of estrogen, on the other hand, declined during the first 3 days and was absent during the next 5 days. On the tenth day a high level of estrogen abruptly reappeared and then declined during the 2 succeeding days.

During the first 9 days of pregnancy the history was essentially the same as that in the same portion of pseudopregnancy. On the ninth day of pregnancy the level of progestin decreased sharply and remained low throughout the rest of gestation, although a slight increase was suggested during the last 4 days. The level of estrogen remained low until the eleventh day when it rose somewhat. Throughout the remainder of pregnancy a moderate level of estrogen was evident. A further but small increase immediately preceded parturition. By 2 days after parturition the action of estrogen had virtually disappeared whereas progestin had attained a high level.

Whether the low level of progestin indicated during the latter half of pregnancy is real or the result of a decreased responsiveness of the endometrium to this hormone is unknown. 3 plates (18 figures).



were more common in the atretic follicles of prepubertal animals than in adults. In order of their frequency, the abnormal manifestations of atretic follicles were (1) ova showing first maturation spindles; (2) ova with two nuclei, the result of either mitotic or amitotic division, a few of which had extruded a polar body; (3) ova with the first cleavage spindle; (4) segmentation of ova, most commonly the two-celled stage; and (5) in one case an atretic ovum with typical morula appearances. Binucleate ova and two-celled cleavage stages were more common in the immature ovary, while in the adult ovary first maturation and cleavage spindles, segmentation and the one example of a morula were found. In an attempt to increase the number of atretic follicles a group of immature animals was treated with gonadotropic hormone and groups of immature and mature animals were given testosterone propionate or oestradiol monobenzoate. These treatments did not appreciably affect the yield of parthenogenic phenomena in the ova of atretic follicles.

## THE VITAMIN C BALANCE DURING PREGNANCY

HERBERT FREDRIKSON

*Acta Obst. & Gynec.*, 25: 1-17, 1945

During the period December, 1942, through November, 1943, the author studied, by titration with dichlorophenolindophenol, the vitamin C content of the blood of pregnant and nonpregnant women in Medelpad, a district in central Sweden. From this investigation it appears that the vitamin C content of the blood is subject to considerable seasonal variation, being, in both groups of women, higher in summer than in winter. The blood ascorbic levels were the same in the nonpregnant and pregnant cases. The study therefore does not provide evidence to support the claim made by numerous investigators that a vitamin C deficiency prevails during pregnancy. Nor was it found that the content of ascorbic acid varies with the stage of pregnancy, independent of seasonal variations. No connection could be established between the vitamin C content and kidney disease or gingivitis.

The vitamin C content of fetal blood was found to be considerably higher than that of the maternal blood, but the two followed a parallel course.

## PLACENTAL GROWTH AFTER FOETAL DEATH IN THE RAT

A. ST.G. HUGGETT AND J. J. PRITCHARD

*J. Physiol.*, 104: 4P, 1945

For these studies fetal death was produced either on the 10th day of pregnancy (one day prior to union between the mesodermal and ectodermal tissues of the

THE OVARIAN INTERSTITIAL GLAND TISSUE AND ITS RELATION  
TO THE PREGNANCY CYCLE IN THE GUINEA PIG

W. T. STAFFORD AND H. W. MOSSMAN

Anat. Rec., 93: 97-107, 1945

Recent literature generally makes a direct approach to ovarian interstitial gland function through endocrinological experiments. This report observes the morphology of the tissue in relation to the reproductive cycle in consideration "that valuable clues to function might conceivably be acquired by such observations."

The authors describe the interstitial gland cells and their arrangement. In the guinea pig most of them are formed from the theca interna of degenerating follicles and most of those of the medulla are the result of the migration of the cortical masses toward the center of the ovary. The cells are in general more scattered in the medulla and larger, and are often more heavily laden with osmiophilic granules.

It was noted that there is no easily observable cycle in character or amount of interstitial gland tissue in the guinea pig ovary that can be correlated with the pregnancy cycle. However, there is a definite trend toward a maximum relative amount of interstitial gland tissue in the cortex near estrum and through early pregnancy with a minimum in mid-pregnancy. The peak and low in the medulla seem to lag a week or so behind those in the cortex, indicating the probable origin of the medullary interstitial tissue from that of the cortex. These observations are in general agreement with previous observations on certain mammals with relatively long reproductive cycles where the changes in interstitial tissue are much more pronounced.

Lack of degeneration phenomena in interstitial gland cells at any stage of the cycle in the guinea pig, and the fairly common occurrence of elongated fibroblast-like stages of these cells, indicates that they do revert to fibroblasts. This would account for the absence of a progressive interstitial cell hypertrophy of the ovary, and would in part account for the gradual increase in fibrous tissue in the ovarian medulla with advancing age. 2 plates (13 figures).

## PARTHENOGENESIS OF ATRETIC OVA IN THE RODENT OVARY

P. BACSICH AND G. W. WYBURN

Jour. Anat., 79: 177-179, 1945

The results of a systematic search over a period of years for evidence of parthenogenesis in a large number of serially sectioned ovaries from adult and immature guinea pigs, rabbits and rats are reported. Parthenogenic phenomena were found in only a relatively small percentage of the ovaries examined. They

three untreated animals of group 4. One of the thyroid-fed animals in this group delivered a number of dead fetuses, and the other two mothers died suddenly on the 26th day of pregnancy. Dissection revealed 13 well developed fetuses in one case and 12 in the other.

## TRANSMISSION OF STREPTOMYCIN FROM MATERNAL BLOOD TO FETAL CIRCULATION AND THE AMNIOTIC FLUID

J. H. E. WOLTZ AND MARJORIE M. WILEY

Proc. Soc. Exper. Biol. and Med., 60: 106-07, 1945

Streptomycin, an antibiotic substance, supplements penicillin by arresting the growth of many of the gram negative bacilli. The purpose of this paper is to demonstrate the concentrations of maternally injected streptomycin in cord blood and amniotic fluid as a preliminary step to an evaluation of its usefulness in the treatment of intrauterine infections.

A single intravenous injection of 250,000 units of streptomycin dissolved in 5 cc. of normal saline was given to each of 14 normal women at term in active labor. Specimens of amniotic fluid, placental cord blood and maternal blood (withdrawn from the antecubital vein of the mother) were collected and streptomycin concentrations were determined. Streptomycin was found to be present in the cord blood and amniotic fluid 19 minutes after intravenous injection into the mother. Streptomycin concentrations in the cord blood and amniotic fluid were generally less than half that found in the maternal blood. Streptomycin concentrations were found to be very low in the specimens of maternal blood, cord blood and amniotic fluid obtained more than 3 hours after injection.

All toxic reactions in the mothers were subjective and transitory. There were no apparent toxic effects on the babies. The conclusion reached by the authors is that streptomycin appears in the cord blood and in the amniotic fluid following intravenous administration to the mother at term.

## UMBILICAL CHANGES DURING PREGNANCY; A FACTOR IN IMPROVING FETAL RESPIRATION AND TRANSMISSION OF FETAL HEART PULSATIONS TO THE ABDOMEN

LOUIS DROSIN

New York State J. Med., 45: 2417-18, 1945

The author shows that while the fetal heart sounds are audible, they are not forcible enough to transmit visible impulses over the maternal umbilical region by way of the fetal chest, liquor amnii and uterine wall.

rat placenta) or on the 15th day. Four methods of killing were used: direct fetal crush at laparotomy, double ovariectomy, injection of oestrone, or injection of follicle-stimulating hormone from mares' serum. In those instances when death occurred on the 10th day a mesoderm-free trophoblast was observed. This trophoblast was differentiated into its three zones with a normal type of evolution, including well developed glycogen accumulation. It grows from a diameter of 0.5 mm. at the 10th day to one of 5.0 mm. at the 16th day, and is destroyed on the 17th day by rupture of maternal vessels into the glycogen zone. In the instances when death was produced on the 15th day, the placenta persisted to full term, growth, however, being restricted to the trophoblast. Ovariectomy and oestrone or follicle-stimulating hormone injections produced either necrosis or absorption of the placental decidua, which, in turn, impaired the growth of the rest of the placenta.

## THE INFLUENCE OF THE THYROID ON PREGNANCY AND PARTURITION IN THE RABBIT

J. P. CHU

J. Endocrinol., 4: 109-114, 1945

Four groups of animals were used in this series of investigations into the relationship between the thyroid gland and gestation in the rabbit. The 11 rabbits of the first group were impregnated and then thyroidectomized at various times between the second and 29th day of gestation. Group 2 consisted of 14 thyroidectomized rabbits impregnated from 17 to 108 days after operation. The four animals of group 3 were given desiccated thyroid at various intervals after thyroidectomy and mated at various times during the period of thyroid feeding. Three of the six animals in group 4 which had been successively thyroidectomized, impregnated and given an injection of pituitary gonadotropin, were treated with 30 mg. of desiccated thyroid per kilogram of body weight every other day. The other three animals of this group received no therapy of any kind following the administration of pituitary gonadotropin.

Very few of the rabbits of group 1 could carry the pregnancy to full term or deliver normal litters. The number of fetuses, however, was in the normal range. When thyroidectomy was performed at an early stage of pregnancy, resorption and abortion of the embryos occurred. Thyroidectomy performed at a late stage of pregnancy resulted in the delivery of still-born young. Pregnancies induced in the thyroidectomized rabbits of group 2 resulted either in resorption of the embryos, abortion, or prolongation of gestation owing to retention of the fetuses. The fetuses of these animals were usually dead at birth. Two of the four rabbits fed with desiccated thyroid following the operation (group 3) gave birth to normal viable litters, while the other two expelled at term dead fetuses which were otherwise normal. Embryo resorption and abortion occurred in the

three untreated animals of group 4. One of the thyroid-fed animals in this group delivered a number of dead fetuses, and the other two mothers died suddenly on the 26th day of pregnancy. Dissection revealed 13 well developed fetuses in one case and 12 in the other.

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The author shows that while the fetal heart sounds are audible, they are not forcible enough to transmit visible impulses over the maternal umbilical region by way of the fetal chest, liquor amnii and uterine wall.

Respiration does not take place in an air-tight, liquor-amnii-filled bag of waters. The only sort of respiration conceivable is endogenous, when the fetus gets an oversupply of oxygen and associated gases, at certain times, which the lungs take up. Such respiration is not apt to register on the abdominal wall through the barriers of liquor amnii and uterine wall. Liquor amnii circulates freely in the lungs at all times. An excess of liquor amnii retained in the lungs, which was not aspirated, is a cause of attacks of cyanosis with imperceptible pulse rates, associated with Cheyne-Stokes respiration. The contractions of labor, which increase the intrauterine tension, have the tendency to express fluid present in the lungs, thus minimizing the incidence of cases showing the bronchial liquor-amnii-retention syndrome.

The vibratory movements of and around the umbilicus are caused by aortic pulsations and vibratory sounds which they produce. The umbilicus is the thinnest, most yielding, and most sensitive part of the abdomen, readily reacting to motion and sound vibrations.

The umbilicus goes through a pattern of evolutionary changes during pregnancy which is followed by a corresponding involution after the termination of pregnancy.

## RELATIONSHIP OF MATERNAL WEIGHT GAIN AND WEIGHT OF NEWBORN INFANT

JACOB S. BEILLY AND IRVING I. KURLAND

Am. J. Obst. & Gynec., 50: 202-206, 1945

The data analyzed in this paper were obtained from the records of 979 private patients delivered at the Beth-El Hospital between January 1, 1942 and December 3, 1943.

These patients were selected according to the following criteria: they began antepartum care before twelve weeks of gestation and were followed regularly to term; they were delivered of a single normal living infant; onset of labor was spontaneous within fourteen days of the expected date of confinement; delivery was by the pelvic route; and they were free of disease during the antenatal period. Well-balanced diet and fluid balance were stressed and occasionally vitamin supplements were given, but no attempt was made to administer treatment with special diets during pregnancy. The low but significant correlation of .184928 was found between the weight gain of the mother and the weight of the baby at birth. It is indicated that every 1-pound gain in the mother's weight is accompanied by a 0.25 pound increase in the baby's birth weight. There is a 68 per cent probability that the birth weight can be predicted on the basis of the mother's gain, within a range of  $\pm 0.9$  pound of the estimated figure. When the data for mothers weighing 100 pounds or less, and 175 pounds or more, before pregnancy, were grouped and compared, it was found that although the gains during pregnancy of the heavier women were not greater than those at the other extreme in weight (19.25 for the heavier and 23.13 pounds for the lighter), they did tend to bear heavier babies.

# MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

## EARLY RISING IN THE PUERPERIUM

G. ROSENBLUM, E. MELINKOFF AND H. S. FIST

J. A. M. A., 129: 849-53, 1945

The data presented by the authors indicate that delivered women can safely and advantageously get up early in the puerperium with no harmful results occurring.

Interesting historical accounts of the practices of various peoples since the biblical Israelites are set forth by the authors. In many tribes, rising on the day of delivery or on the following day was the accepted custom. In 1793 the English obstetrician, Charles White, wrote that frequent upright posture was important in preventing the lochia from stagnating, the stools and urine from being too long retained, and in promoting the contraction of the uterus and of the abdominal muscles. More recently, large numbers of women have been permitted to arise early, at varying intervals according to their condition, and to be discharged as early as the fourth day. No complications have resulted and evident benefit to the patient has been reported.

The practice of early ambulation of surgical patients, now a widely accepted procedure advocated in both American and foreign literature, must be considered intimately related to the practice of early puerperal rising. The objectives and underlying principles of the two are identical. Excellent results have been reported in several hundred surgical patients who were got up during the first 24 hours following operation. Many observers have noted a definite decrease in the minute volume respiratory exchange results from such factors as the depression caused by preoperative medication. This decrease is much more pronounced during the first 24 postoperative hours. Spirometer readings have shown that vital capacity returned to normal much sooner after early rising. One of the authors has advocated and practiced since 1940 the early ambulation of gynecological patients and also advised the use of the transverse abdominal incision in obstetrics and gynecology since patients so operated on may advantageously be made ambulatory within 24 hours.

The authors believed that the objections to early ambulation raised by both doctors and patients were more theoretical than actual. Therefore they attempted to evaluate them accurately. A total of 582 obstetric patients were divided into the following groups: (1) early risers: ambulatory on first or second postpartum day; (2) intermediate risers: ambulatory on third or fourth postpartum day; and (3) late risers: ambulatory later than the fourth postpartum day. In the entire series no changes in delivery or operative technic were made. All patients delivered vaginally remained in the hospital six to eight days while those delivered by cesarean section remained eight to ten days. There were no serious complications in the entire series of 582 patients.

An analysis of the statistics on this series reveals that about 35 per cent of the early risers required catheterizations averaging 3 per patient, while about 40 per cent of the intermediate and 40 per cent of the late risers required an average of 4 per patient. There were 5 cases of urinary infection, all occurring in the intermediate and late groups. Less frequent abnormal bleeding is shown in the early group. Uterine involution was uniformly good in all groups. The fear of breakdown of episiotomy or abdominal wound incisions is unfounded. More efficient mobilization of the bowels is evident, over 3 times as many spontaneous movements occurring in the early group as in the late group. The claim advanced by some that early rising may cause later prolapsus and retroversions is also disproved. There was a decided reduction in the amount of nursing care required for the patients arising early. In the case of cesarean sections, less abdominal distention and discomfort and a much more rapid convalescence were noted. The majority of the patients exhibited enthusiasm, particularly the multiparas, who stated that they felt better and stronger than after previous confinements in which they had spent 7 to 14 days entirely in bed.

It is the hope of the authors that this study will encourage further interest and continued observation on the question of early puerperal rising which may eventually clarify this still unsettled problem.

## THE PLACE OF PROTEIN IN THE DIET OF THE PREGNANT PATIENT

M. BLAIR, MERLE T. PORTER AND L. A. ATKINSON

Canad. M. A. J., 53: 434-37, 1945

Until recent years too little attention has been given to the importance of protein in the diet of the pregnant patient. Today the medical profession is more cognizant of its importance. Protein is essential to growth and growth begins with conception, not birth.

The Committee of Foods and Nutrition of the U. S. National Research Council has estimated the need of the average case during the last half of pregnancy to be 85 grams per day. The authors believe that this figure should be taken as a minimum and that a safer figure is between 100 and 120 grams per day.

The three basic causes of protein deficiency are offered by the authors as follows: (1) A lowered protein intake has been recommended in the past at the first sign of trouble. It is now realized that protein in quantity is both necessary and essential to the pregnant patient. Eclampsia is the only condition that should suggest a lowered protein intake; (2) Increased protein need is felt by the mother in early pregnancy and increases with fetal growth. A definite relationship is suggested between the protein content of the mother's diet and the birth length and birth weight of the baby. However, the length of labor does not vary between adequate protein intake and larger babies and inadequate protein intake and smaller babies; and (3) Increased protein loss is most commonly due

to its excretion through the kidneys. The appearance of proteinuria should not be a signal to lower protein intake, but should indicate that plasma proteins be kept up.

The authors discuss the relation of water balance and edema to the toxemias of pregnancy. It has been observed that the lower the serum proteins, particularly albumin, in the intravascular system, the greater the edema; and conversely, as the intravascular serum proteins increase the edema disappears.

The tendency for anemia to appear during the last six months of pregnancy is common knowledge. It has been shown in dogs that there is a relationship between low protein intake and low hemoglobin. It has been demonstrated that this is also true of pregnancy cases. It is also believed that where there is a rich protein diet during pregnancy there is an improvement in the supply of breast milk.

To keep the protein intake at a high level is not easy both because the average sedentary patient does not enjoy an abundance of meat, fish, milk and eggs and because such foods are costly. In attempting to find some method of protein intake other than food, commercial amino-acid products were examined and rejected because of taste, odor or price. Consultation with commercial milk companies revealed that skim milk powder most nearly met the need. This product is cheap as well as tasteless and odorless and the protein content is 2.41 grams per level tablespoon. A set of recipes has been evolved using skim milk powder.

The authors present a high protein diet which they have used consistently and which they consider practical because it is edible. This diet consists of 120 grams of protein, 50 grams of fat, 300 grams of carbohydrates and 2,130 calories. It avoids excessive salt, fried foods and rich foods, but includes large amounts of protein in the form of lean meats, fish and fowl, eggs, cheese and milk.

(See editorial note following next abstract.—Ed.)

## MEAT IN THE DIET OF PREGNANT WOMEN

RUTH M. LEVERTON AND THELMA J. McMILLAN

J. A. M. A., 130: 134-136, 1946

Because of the widespread inadequacy of the protein intake of pregnant women it is desirable to find some simple dietary recommendation which if followed would be effective in increasing their protein intake. The study reported has tested the effectiveness of the recommendation "Eat plenty of meat—a generous serving at least twice a day." Though such a recommendation is definitely uncommon, it has the advantage of being easy to follow as well as furnishing an appreciable amount of several nutrients. Women whose intake of protein was augmented by receiving a 5 ounce serving of meat daily in addition to their self-chosen diets during the period from four months before delivery until three

months after delivery had higher hemoglobin and red cell values, less edema and better success in lactation than women who received a supplement of B complex or women who received no supplement. The results indicate that the recommendation to normal pregnant women to increase their protein intake by eating a generous serving of meat daily in addition to their self-chosen diets would be effective in increasing hemoglobin and red cell concentration, avoiding edema and promoting lactation.

(A number of articles published in the last few years have correctly stressed the importance of liberal protein intake in pregnancy and have deprecated the low protein consumption of many gravidæ. But the opposite opinion was widely and staunchly held until very recent years and has not yet been entirely dispelled. Indeed, to my knowledge, not a few physicians are still restricting meat intake in pregnancy on the grounds that it predisposes to toxemia of pregnancy. This old bug-bear, which held rather general sway until the early thirties, had its genesis in the 19th century belief that eclampsia and pre-eclampsia were allied to uremia. We all know now, of course, that even in these acute toxemias patients show no impairment of the kidneys to excrete nitrogenous substances and, when studied by the most delicate tests, eliminate urea with ease.

The idea that a high meat intake in pregnancy predisposes to toxemia received its greatest impetus, perhaps, in World War I when it was observed that the incidence of eclampsia was greatly reduced in those geographical areas affected by the "food blockage" and rose again after the war and food blockade ended. Everyone in these localities, including pregnant women, had to exist on a diet which was very low in protein and fat and correspondingly high in carbohydrate. The inference was accordingly drawn that the diminution in eclampsia in these areas was due to a reduction in meat consumption. Subsequent statistical studies, however, have shown that in these war-ridden territories, almost all young husbands were away at the front and that, as a result, there was great decrease in first pregnancies. Since pre-eclampsia and eclampsia are particularly prone to affect young primigravidae, a reduction in the general incidence of the disease would be expected under these circumstances. Moreover, in those first pregnancies which did occur, the incidence of eclampsia showed no change. In other words, meat intake had nothing to do with the reduction in the incidence of this disease.

Because of its wide dissemination among physicians and laity alike, the old fear that meat is harmful in pregnancy will only be quelled after much hammering on the subject. Accordingly, the two articles abstracted above which adduce new evidence in support of the value of a high protein intake in pregnancy are timely and welcome.—Ed.)

## CONTINUOUS CAUDAL ANESTHESIA AS AN ANALGESIC AND THERAPEUTIC AGENT

G. J. ELLIS AND J. B. SHEFFREY

Anesth. & Analg., 24: 193-204, 1945

The authors evaluate continuous caudal anesthesia in respect to safety and effectiveness as an analgesic and therapeutic agent. Up to the present time, there have been over 47,000 continuous caudal anesthetics administered, with 19 reported deaths. The 19 cases are presented in this report; 9 of them are considered anesthetic deaths and 10 are judged to be obstetrical or medical deaths

unrelated to the anesthetic. Of the 9 anesthetic deaths, some probably could have been avoided with proper technique and adequate supervision. The corrected anesthetic death rate is 9 cases in 47,000, an incidence of 1 death in every 5,222 cases. Comparing this incidence with that of the maternal anesthetic death rate as a whole, it was found that in a group of cases where every anesthetic except caudal was used, the incidence was 1 death in 3,453 cases. It is concluded that caudal anesthesia is no more dangerous than other forms of anesthesia.

The authors prefer the fractional method with a malleable needle which is discarded after using 5 times. With this method, danger of needle breakage is minimal. The technique is described with emphasis upon inserting the needle to the hub. If cerebrospinal fluid appears or can be aspirated the needle is withdrawn and the patient considered unsuitable for this type of anesthesia.

There are certain specific conditions in which caudal anesthesia should be the anesthetic of choice. These are prematurity, heart disease, chest disease, renal disease, toxemia of pregnancy, cervical dystocia and full stomach at time of delivery. When the indication presents itself, caudal anesthesia may be used in cesarean section.

Caudal anesthesia is contraindicated in the following conditions: (1) nervous and apprehensive patients who border on the hysterical; (2) when obesity makes the sacral hiatus difficult to palpate; (3) when a history of quick labors in a multigravida frequently will not allow sufficient time before delivery for the anesthetic to take effect; (4) when there are anomalies or infections about the sacrum; (5) in cases of placenta previa or premature separation; (6) when there is cephalo-pelvic disproportion; and (7) when, after previous cesarean section, the patient is allowed to have a trial labor.

The obstetric patient is found to be in better condition than when delivered under any other form of anesthesia. The incidence of cerebral accidents in the newborn is decreased. Since the child is not narcotized by the anesthetic, it cries readily and resuscitation is rarely necessary. Caudal anesthesia tends to shorten both the first and second stages of labor and third stage blood loss is definitely decreased.

In sixteen cases of acute pelvic thrombophlebitis, block of the lumbar sympathetic chain by continuous caudal anesthesia has proved a useful therapeutic method.

## THE TWO MAIN DIAMETERS AT THE BRIM OF THE FEMALE PELVIS

C. NICHOLSON

J. Anat., 79: 131-35, 1945

The author has found that the figure quoted in text-books of anatomy for the conjugate diameter of the female pelvis is too low. His findings are based upon

an analysis of pelvimetry by radiology in 640 cases at Moreton-in-Marsh District Hospital.

The population represented in this series consisted of all primigravidae, constituting a fair sample of a mixed rural population which is more genetically and socially homogenous than that derived from city populations. It was found that the mean diameter for this group was a half inch larger than that quoted in text-books. The diameter of the female pelvis is very sensitive to nutrition and the text-book figure was probably derived from measurements of cadavers of the lowest social level. In the present series, the mean conjugate diameter was established as 120.19 mm. and the mean transverse diameter as 131.30 mm. 5 references.

## VALUE OF SUPPLEMENTS OF VITAMIN C IN PREVENTING LACTATIONAL MASTITIS

A. A. FULTON

Brit. M. J., p. 488-91, 1945

This article deals with experiments made in an effort to determine whether lactational mastitis might be due to vitamin C deficiency.

The patients of two ante-natal clinics were used in the study. These clinics were attended by patients similar in most respects, including social status. The expectant mothers attending clinic A, 124 in number, were given a daily supplement of ascorbic acid from the sixth month of pregnancy until the end of the sixth month after delivery, thus covering the later months of pregnancy and almost the whole period of lactation. These supplements consisted of 50 mg. tablets, one a day for the time mentioned. The dosage was based on the daily requirement of 30 mg. for an adult, 20 mg. surplus being allowed on account of the increased demands of pregnancy and lactation. The total daily intake was probably about 70 mg., as the women presumably were consuming some vitamin C in their ordinary diet. Those patients attending clinic B received no supplement.

The results of the study indicated that vitamin C administration per se has no influence on the incidence of mastitis.

## PATHOLOGY OF PREGNANCY

### HEMORRHAGE AS THE MOST FREQUENT CAUSE OF MATERNAL DEATH. AN ANALYSIS OF THE PUERPERAL DEATHS IN BROOKLYN, 1944

CHARLES A. GORDON

Amer. Jour. Surg., 70: 277-282, 1945

In New York City 132,735 births were recorded in 1944. Of these the largest number (51,082, including 3,502 non-white) occurred in the Borough of Brooklyn. In this year the puerperal mortality rate per 10,000 reported terminated pregnancies, standardized for color, declined to a new low level in the entire city, that is, to 16.6, and in Brooklyn to 12.4, the lowest rate for the 5 boroughs.

The causes of the 62 puerperal deaths in Brooklyn were officially assigned as follows: abortion, 10; ectopic pregnancy, 3; hemorrhage, 8; toxemia, 11; infection, 20; other diseases and accidents, 8; all other, 2. A further analysis of the records revealed that hemorrhage was the actual cause of death in no less than seven of the abortions. In one case death followed sudden profuse hemorrhage two days after spontaneous abortion; in two cases severe hemorrhage occurred during removal of retained tissue; and in one case profuse and repeated hemorrhage caused death after vaginal hysterectomy for missed abortion. In all three cases of ectopic pregnancy intraperitoneal hemorrhage was great; in two the cause of death was discovered at autopsy.

In the group of deaths attributed to toxemia, one case was directly due to anesthesia and in two cases hemorrhage was an important factor in death.

The infection group contained a number of cases difficult of exact assignment to any one particular cause of death. The trauma and shock of operative pelvic delivery were important factors in two cases in which hemorrhage apparently was not significant. Severe hemorrhage occurred in seven cases in this group; one of these was associated with rupture of the uterus.

Cesarean section contributed to death in eight cases. In one case of placenta previa associated with profuse antepartum hemorrhage, 250 cc. of blood were administered nearly three weeks after operation; death several weeks later was directly due to infection. In two other cases death within one hour after operation was attributed to shock. Plasma was administered, but blood was not available for these women.

Included in the accident group were six cases of rupture of the uterus, which appears to be a more important cause of death than is generally appreciated. Blood replacement in this group was inadequate. Blood was given in only one case and in two plasma was administered.

Although statistically hemorrhage was assigned as a principal cause of the death in only eight cases, and in three others was coded as a secondary cause, the

author, from an analysis of the case records, was able to classify 35 deaths as due to this cause, although in some of these cases death may have been finally due to embolism, peritonitis or some other form of infection. His group includes only those cases in which hemorrhage was reported to have been profuse or severe, or when the uterus was packed or ruptured; it excludes cases of shock or sudden death if the record stated that blood loss was moderate or not excessive.

In only two of the eight deaths officially attributed to hemorrhage was blood administered; in two others plasma was given and in one other case blood was available but not compatible.

From this study the author concludes that maternal mortality could be further reduced by greater emphasis on control of hemorrhage. For treatment of serious obstetrical hemorrhage, blood plasma is not sufficient. Large amounts are often necessary and speed during actual administration is often vital. In the emergency when veins fail, or cut-down proves time consuming or unsuccessful, sternal transfusion is safe and effective.

(Gordon deserves much credit for his emphasis on hemorrhage as the outstanding cause of maternal death because it certainly is. In addition to cases in which the patient actually bleeds to death, there is an equally important group in which the patient manages to escape death from exsanguination but dies some days later from puerperal infection. Although autopsy findings as well as the International List of Causes of Death may classify such fatalities under infection, it is indubitably clear that the factor primarily responsible for most of these deaths is exsanguination abetted by the intra-uterine manipulations made necessary by the bleeding. Not only does massive blood loss in itself predispose both to infection and shock, but many of the measures employed in the treatment of hemorrhage, such as manual removal of the placenta and uterine tamponade, introduce infection, inflict trauma and often require prolongation or renewal of anesthesia.—Ed.)

## ABORTION

JAMES GILMOR

Clinics, J. B. Lippincott Co., 4: 664-675, 1945

This article comprises a succinct review of present-day knowledge of the causation of abortion followed by a description of the author's methods of managing the different varieties of this complication.

In threatened abortion it is the author's custom to put these patients at absolute rest in bed, to elevate the foot of the bed, and to give opium. He prefers tincture of opium by mouth because he feels it decreases the irritability of the uterus, has a sedative effect upon the patient and in most instances decreases peristalsis. Lutein should be given at once. If there is much pain present 10 cc. are given intravenously followed by 10 cc. intramuscularly every four hours. When no bleeding follows the initial blood loss and cramps are controlled the lutein can be reduced to 10 cc. intramuscularly twice a day. Also thyroid

by mouth is given in small doses unless the patient is known to be a definite hyperthyroid. It is advisable to avoid all local applications to the abdomen or the pelvis, especially ice. It is the author's feeling that ice, should the cold reach the uterine musculature, is likely to cause contractions and should be avoided. The remainder of treatment is to continue this regime as initiated for a maximum of four days when it can be gradually relaxed. It is advisable that these patients have no bowel movements for five or six days after which time they can be given mineral oil in one of its many forms, by mouth, and a low oil enema. It is also recommended that these patients be not examined until all signs of symptoms of threatening have disappeared, and then only very superficially and only if entirely necessary for differential diagnosis. In discussing incomplete abortion the author refers to the patient who has previously been seen in the home and because of bleeding has had the vagina packed with anything available at the time. This has usually been done hastily and always in a dirty manner, with little or no local preparation of the patient. He mentions this only because of the uselessness and danger of the procedure. These women can occasionally bleed to an alarming degree, but a vaginal pack alone never stopped one, and is dangerous under the circumstances from the standpoint of infection.

## CRIMINAL ABORTION: THREE CASE REPORTS

THEODORE CIANFRANI

Am. J. Surg., 70: 100-04, 1945

Because of the meagerness of reports of criminal abortions in recent years, the author believed it appropriate to report three such cases.

The first case in which an eyebrow tweezer was used in an attempted criminal abortion emphasizes the need of thorough study of x-rays to ascertain the direction of such a double-pronged sharp instrument, so vitally important in its removal. A flat film is not adequate because of the variation in position of the uterus. The relationship of a foreign body to the uterus is the important factor and not its relationship to the bony pelvis.

The other two cases were attempted criminal abortions by the passage of glass cocktail stirring rods into the uterus. In each case the rod perforated the uterine wall and entered the abdomen with no interruption of the pregnancy. These cases illustrate: (1) the ease with which foreign bodies can perforate a uterus without unduly alarming the patient with pain or hemorrhage; (2) the amount of trauma a pregnant uterus can stand without causing it to abort; and (3) the efficacy of modern drug therapy and early operation.

These cases show to what lengths some women will go to rid themselves of an undesired pregnancy. The trend in modern times has been instrumental interference by a trained abortionist. In spite of danger of infection, cauterizing ae-

tion and the risk of pushing the solution through the tubes into the abdomen, the intrauterine injection of soap solution or glycerine seems to be the preferred method. The commonest accident of illegal abortion is perforation of the uterus, with infection usually added. In these cases, laparotomy is advised as soon as possible because of potential infection. 4 references. 4 figures.

## FETAL BONES PASSED IN THE FECES

BEN FRUHLINGER

Am. J. Surg., 70: 126-27, 1945

The author reports the case of a 26-year-old woman who entered the hospital complaining of severe pain in the lower right quadrant of the abdomen with a temperature of 104.8. The history revealed that she had been treated previously for moderately advanced pulmonary tuberculosis and her left lung collapsed. A therapeutic abortion was performed about twelve days prior to the present admission. The attending surgeon stated that fetal parts were removed by curettage, indicating that the pregnancy was intrauterine.

A curettage was performed at this hospital and no material recovered, but a foul-smelling bloody vaginal discharge persisted for a few days. On the eighteenth postoperative day, examination of the feces revealed a small number of bony particles. An exploratory laparotomy was performed which showed numerous pelvic adhesions and an abscess lying posterior to the uterus. A teaspoonful of pus was removed from the abscess and this pus contained bony particles similar to those found in the feces. The bony particles from both the feces and abscess were reported to be bones from a human fetus about fifteen weeks old. 3 references.

## FULL-TERM EXTRA-UTERINE PREGNANCY ASSOCIATED WITH EXTENSIVE PROLAPSE

R. G. MORGAN AND NORA L. KEEVIL

Brit. M. J., 2: 649, 1945

The authors report the following case of a full-term extra-uterine pregnancy associated with extensive prolapse which shows many points of interest in addition to its rarity. There was complete lack of symptoms pointing to an early emptying of the uterine contents into the abdominal cavity. Toxemia occurred at 36 weeks' gestation. A persistent transverse lie and extensive prolapse were aids to the diagnosis.

The patient, a 41-year-old woman, 7-para, reported to the antenatal clinic when four months pregnant. Her only complaint was "dropping of the womb." Examination revealed the fundus enlarged to the size of a 16 weeks' pregnancy, extensive prolapse and a slightly eroded cervix. A large ring pessary was inserted.

The pregnancy progressed, but the pessary was unsatisfactory. The cervix was now ulcerated and bleeding and the patient was admitted to the hospital where she improved and was fitted with a Napier's pessary. At about one month before term she was readmitted to the hospital with toxemia of pregnancy.

The fetus at this stage was lying in a transverse position high up in the uterus. Attempts at version were immediately successful. X-ray study reported a single pregnancy, transverse presentation, spine upwards, the head being opposite and above the left iliac crest. Extra-uterine pregnancy was suspected and at this time the patient began to have violent abdominal pain, vomiting and a rapid rise in pulse rate. A laparotomy was performed and a live baby delivered which died about an hour later.

The umbilical cord was about 18 inches long and its distal half was divided into two separate vascular bundles separately entering the placental mass. The latter had an extensive attachment in the pelvis involving the peritoneal surfaces of the bladder, cecum, enlarged uterus and broad ligaments. The placenta was removed and the patient had an uneventful convalescence.

(A combination of what was evidently a nearly full term secondary abdominal pregnancy with a living child, with also prolapse and toxemia, is not a pleasing offering to any obstetrician, but the outcome in this case appears on the whole to have been a happy one. It is rather casually remarked that the placenta was removed, which with a living child is likely to be a hazardous procedure, with usually dangerous bleeding. Many would probably have chosen to leave it for absorption or to marsupialize it, the former method being the more desirable in most cases. And yet no mention is made of any unusual bleeding in this case report, and the convalescence was apparently uneventful.—Ed.)

### SIMULTANEOUS RUPTURED TUBAL PREGNANCY AND INTRA-UTERINE PREGNANCY WITH SUBSEQUENT DELIVERY OF A NORMAL INFANT

G. TURNER HOWARD, JR.

South. M. J., 38: 788-89, 1945

Two other cases of simultaneous intra-uterine and extra-uterine pregnancy have been found in literature and the following case is described by the author to be added to those previously reported.

The patient, a 28-year-old woman, was admitted to the hospital with the complaint of intermittent cramp-like abdominal pain for 4 weeks, worse in the left lower quadrant and becoming progressively more severe. Examination re-

vealed a well developed woman in no distress or pain. Both lower quadrants of the abdomen were moderately tender, especially the left. The uterus was found to be enlarged to the size of a grapefruit, smooth and soft. Motility of the cervix was painful and there was definite tenderness and some thickening in the left vault. A brownish discharge was present from the vagina.

While the report from a Friedmann test was awaited, the patient had an attack of severe spasmodic pain in the left lower quadrant and an immediate operation was performed. A ruptured ectopic pregnancy was found in the left tube. The uterus was enlarged to the size of a  $2\frac{1}{2}$  months pregnancy and was otherwise normal. The left tube and ovary with the ectopic products of pregnancy was excised with care not to traumatize the uterus. The appendix was removed and the pelvis gently cleaned of all clots.

Seven months after operation, the patient was delivered of a normal female child by an obstetrician in another city.

## BILATERAL TUBAL PREGNANCY AND SIMULTANEOUS INTRAUTERINE PREGNANCY; CASE REPORT

ALFRED HORCHLER

Zentralbl. f. Gynäk., 68: 366, 1944

Two months after her last menstrual period the patient was admitted to the hospital for hemorrhage and colic-like pains in the left lower abdomen which were so severe as to cause fainting. At operation both tubes appeared irregular in form and contained parasalpingitic adhesions. Pregnancy was evident in the left tube and suspected in the right tube, a suspicion which was confirmed at later examination. Both tubes were removed. The uterus appeared enlarged and slightly retroverted. Ventro-suspension of the uterus was performed. Corpus luteum hormone preparations were administered and the patient's recovery was uneventful. Three weeks after discharge from the hospital she aborted an intra-uterine conception.

## INTERSTITIAL PREGNANCY

WENNER (BASEL)

Monatschr. f. Geburtsh. u. Gyn., 119: 167-168, 1945

In August, 1944, a 27-year-old woman entered the hospital with the picture of an acute ruptured tubal pregnancy. Her last menstrual period had been July 1, 1944. In 1937 her left ovary and tube had been removed because of an ovarian

cyst. In 1941 she had a normal pregnancy. A laparotomy was performed immediately. A profuse amount of watery and coagulated blood was found in the abdominal cavity. The omentum was adherent to the parietal peritoneum and to the left fundal angle. The right tube and ovary were entirely normal, the left were absent. The fundal angle was distended and bluish and a small ruptured place from which the chorial tissue protruded was found on the posterior wall. This part was excised without opening the uterine cavity, and sutured. The postoperative course was normal. The histological picture showed a typical interstitial pregnancy and some glandular ducts as in salpingitis isthmica nodosa were seen on the tube. An inner migration of the fertilized ovum is assumed.

(We had an identical case a year or so ago and likewise interpreted it on the grounds of internal migration of the ovum.—Ed.)

## LEIOMYOMA OF THE OVARY COMPLICATING PREGNANCY

JOHN H. MOORE

*Am. J. Obst. & Gynec.*, 50: 224-226, 1945

The author's search of the literature revealed only two instances of leiomyoma of the ovary complicating pregnancy. In one of these, reported by Olshausen in 1907, operation was performed in the third month of pregnancy, the patient carried to term and gave birth to a mature living child. In the other case, reported by Brachetto-Brian and Casco in 1941, histological study of the left ovary removed at operation for pelvic appendicitis, established the diagnosis of pregnancy in the cortical zone of an organ showing generalized endometriosis. The embryo was not found. The present report deals with a married white woman, 34 years of age, who was admitted to hospital with a diagnosis of pelvic tumor complicating a pregnancy of a little over two months. An abdominal incision revealed a solid tumor (1,170 grams) of the right ovary and a right ovariectomy was performed. The patient was discharged on the fourteenth day after operation. The pregnancy developed normally; delivery of a boy weighing 7 pounds, 8 ounces followed an uneventful labor, and the mother's postpartum course was normal. Microscopically, the tumor was of uniform structure throughout. It was composed of adult smooth muscle with a moderate amount of collagenous tissue between the muscle fibers. The microscopic diagnosis was benign leiomyoma.

HYPERNEPHROID CARCINOMA OF THE KIDNEY OR ADRENAL (?)  
AND PREGNANCY

A. F. LASH

Am. J. Obst. &amp; Gynec., 50: 221-223, 1945

Few cases of renal tumors as a complication of pregnancy have been reported in the literature. Pregnancy is influenced by this group of tumors, hypernephroid carcinoma (or clear-cell adenocarcinoma) only as a mechanical factor producing pressure on the kidneys or ureters. It is pointed out that these and other uterine adnexal or extrapelvic masses can easily be overlooked at the time of lower uterine segment cesarean section because of the restricted field of operation.

The case reported in the present paper illustrates this fact. The patient, a 30-year-old white primigravida was admitted to hospital because of hypertension and albuminuria at term. During the course of pregnancy she had transient rises of systolic blood pressure varying from 148 to 172. Urinary findings were normal. At hospital she was placed on a strict regime of bed rest, low-protein, salt-free diet, daily magnesium, and sedation. Since after three days no improvement occurred and medical induction of labor failed, a lower uterine segment cesarean section was performed and a normal male child, weighing 6 pounds, 14 ounces, was delivered. Seven days later the patient complained of right abdominal pain and became febrile. On physical examination a large cystic mass was found and tentatively diagnosed as a right ovarian cyst or an acute cystic degeneration of a pedunculated fibroid. Since neither sulfadiazine nor penicillin therapy changed the febrile course, surgical laparotomy was made 35 days after the cesarean section. A large retroperitoneal mass, originating from the upper portion of the right kidney was found and removed. Microscopic examination showed hypernephroid carcinoma with tremendous hemorrhage and necrosis and the formation of cyst-like hematoma. The patient made an uneventful recovery.

## NEPHRITIS AND THE CONTRAINDICATION OF PREGNANCY

EDMUND LISSACK

Urol. &amp; Cutan Rev., 49: 553-554, 1945

The author reports the case of a woman with recurrent nephritis whom he conducted through four consecutive pregnancies, all of which resulted in the delivery of living and healthy children. Since an attack of pyelitis in 1932, however (the first child was born in October of that year), her kidneys had caused her trouble nearly every month near the menstrual time. This would commence with yawning, followed by a hard chill and in turn by vomiting. High fever

and also weakness would usually follow. Pains in the mid-back and especially over the kidney regions were common. The patient made uneventful recoveries in the first three pregnancies but died in the last.

Permission to terminate the fourth pregnancy was not granted on religious grounds. Rest in bed was advised and frequent functional tests were made from the fifth month of pregnancy when she entered hospital. A bilateral retrograde pyelogram taken early in the fifth month of pregnancy showed each kidney pelvis markedly enlarged, the calices and infundibuli enlarged and dilated, and the ureters greatly enlarged. The blood pressure was 200/100 and rose to 260/100 before delivery; the urine contained a trace of albumin. Blood chemical findings were normal. The output of phenolsulphonphthalein in two hours was 37 per cent. After delivery of a healthy boy by cesarean section, convalescence was fairly normal. The wound healed nicely, but albumin continued to be found in the urine, the blood count stayed low, and the blood pressure continued over 200 with a diastolic of 120 to 130. The nephritic condition could not be lowered because of the damage already done to the renal tissue. She died a month after delivery, as a result of the pregnancy strain on the previously existing nephritis.

## NEPHROLITHIASIS AND PREGNANCY

FREDERICK H. FALLS

Urol. & Cutan. Rev., 49: 548-552, 1945

Kidney stones complicating pregnancy and producing serious symptoms are quite rare. The atony and dilatation normally seen in the upper portion of the ureter during pregnancy predisposes to the passage of stones to its distal end. Here the thickening of the smooth muscle sheath of Waldeyer, due to hypertrophy coincident to pregnancy narrows the lumen, and interferes with the passage of a stone into the bladder. The inhibition of ureteral peristalsis shown by many observers which occurs during pregnancy also may play a part in preventing renal colic, and the passage of a ureteral stone. This inhibition is thought by some to be due to the anti-peristaltic action of progesterone. The decreased peristalsis may, by permitting stagnation of the urine in the ureter, predispose to the formation of kidney stones by favoring precipitation of urinary salts on any foreign body present in the pelvis of the kidney, such as epithelial cells, bacteria or pus cells.

Since the formation of kidney stones is frequently dependent upon infection of the pelvis of the kidney, when a kidney stone complicates pregnancy, an associated pyelitis, which has been dormant before the start of pregnancy, may light up and produce typical symptoms. As a result, in all cases of pyelitis of pregnancy, an x-ray should be taken to rule out the presence of a kidney stone.

HYPERNEPHROID CARCINOMA OF THE KIDNEY OR ADRENAL (?)  
AND PREGNANCY

A. F. LASH

Am. J. Obst. &amp; Gynec., 50: 221-223, 1945

Few cases of renal tumors as a complication of pregnancy have been reported in the literature. Pregnancy is influenced by this group of tumors, hypernephroid carcinoma (or clear-cell adenocarcinoma) only as a mechanical factor producing pressure on the kidneys or ureters. It is pointed out that these and other uterine adnexal or extrapelvic masses can easily be overlooked at the time of lower uterine segment cesarean section because of the restricted field of operation.

The case reported in the present paper illustrates this fact. The patient, a 30-year-old white primigravida was admitted to hospital because of hypertension and albuminuria at term. During the course of pregnancy she had transient rises of systolic blood pressure varying from 148 to 172. Urinary findings were normal. At hospital she was placed on a strict regime of bed rest, low-protein, salt-free diet, daily magnesium, and sedation. Since after three days no improvement occurred and medical induction of labor failed, a lower uterine segment cesarean section was performed and a normal male child, weighing 6 pounds, 14 ounces, was delivered. Seven days later the patient complained of right abdominal pain and became febrile. On physical examination a large cystic mass was found and tentatively diagnosed as a right ovarian cyst or an acute cystic degeneration of a pedunculated fibroid. Since neither sulfadiazine nor penicillin therapy changed the febrile course, surgical laparotomy was made 35 days after the cesarean section. A large retroperitoneal mass, originating from the upper portion of the right kidney was found and removed. Microscopic examination showed hypernephroid carcinoma with tremendous hemorrhage and necrosis and the formation of cyst-like hematoma. The patient made an uneventful recovery.

## NEPHRITIS AND THE CONTRAINDICATION OF PREGNANCY

EDMUND LISSACK

Urol. &amp; Cutan Rev., 49: 553-554, 1945

The author reports the case of a woman with recurrent nephritis whom he conducted through four consecutive pregnancies, all of which resulted in the delivery of living and healthy children. Since an attack of pyelitis in 1932, however (the first child was born in October of that year), her kidneys had caused her trouble nearly every month near the menstrual time. This would commence with yawning, followed by a hard chill and in turn by vomiting. High fever

be crushed and removed easily through an operating cystoscope. If the stone lodges in the ureter and will not pass, injections of oil may help to dislodge it and permit passage. The tendency of these stones to lodge in the lower end of the ureter in most cases facilitates their removal by this method.

Stones causing severe colic and not dislodged by this treatment may have to be removed surgically. When operative removal is contemplated the possibility of an abortion resulting therefrom must be kept in mind. To minimize the danger of this it is advisable to inject one of the potent preparations of corpus luteum extract.

During labor these stones cause practically no trouble. Theoretically one might expect that there would be compression of the ureter by the head in the second stage. Practically, the author does not feel that this is an occurrence that may be frequently expected and no post-delivery damage to the ureter from this complication has been recorded.

Eight cases observed at the Research and Educational Hospital in Chicago are presented. In some patients there was marked evidence of associated pyelitis and infection. In others all symptoms were absent and the finding of a stone was accidental. An analysis of this small group of cases and others reported in the literature suggest that: (a) the right kidney and ureter seem to be involved more frequently than the left; (b) the presence of a kidney stone rarely presents serious complications to pregnancy, even in the presence of an associated pyelitis; (c) conservative treatment will in most cases control symptoms and permit of delivery of a viable baby; (d) some cases may go through pregnancy with no symptoms suggestive of kidney stone and develop renal colic only after delivery; (e) women with symptoms of pyelitis or nephrolithiasis should be carefully examined roentgenographically and urologically and by an obstetrician and the stone removed before pregnancy is undertaken.

(This article has been reviewed in considerable detail not only because it is an excellent clinical survey of the subject but also because, as far as I know, it is the only comprehensive consideration which nephrolithiasis in pregnancy has received.—Ed.)

#### STUDIES ON HYPERTENSION. IV. BIOASSAY OF VASOCONSTRICTOR SUBSTANCES IN ULTRAFILTRATES OF CITRATED BLOOD PLASMA FROM PATIENTS WITH NORMAL BLOOD PRESSURES, PATIENTS WITH ESSENTIAL HYPERTENSION AND PATIENTS MADE HYPERTENSIVE BY INTRAVENOUS INJECTIONS OF ANGIOTONIN (HYPERTENSIN).

RAYMOND GREGORY, PAUL L. EWING, WILLIAM C. LEVIN AND GRIFF T. ROSS

Arch. Int. Med., 76: 11-21, 1945.

This report deals with a study of whether vasoconstrictor substances are present in increased amounts in the blood of patients with hypertension. The

The symptoms of kidney stone are not as a rule modified greatly by the presence of pregnancy. An x-ray picture will show the stone without difficulty if it is in the pelvis or upper part of the ureter. However, if the pregnancy is near term, and the stone is low in the ureter, the fetal skeleton or the maternal pelvic bone shadows or both may obscure or mask the shadow of the stone. In this connection it is well to remember that approximately two per cent of the kidney stones, because of their composition, do not show in an x-ray picture.

In early pregnancy vaginal examination or rectal palpation may reveal the stone in the lower ureter. Bimanual palpation of the lower ureter is not difficult in patients who are not obese and who are not so nervous that they cannot relax their abdominal muscles. They are best felt in thin multiparae with well relaxed abdominal walls. Two fingers of the vaginal examining hand are inserted up to the cervix, and then directed upward and laterally. The abdominal hand depresses the lateral fornix and the ureter is felt as a cord running upward and laterally about one inch from the side wall of the cervix and uterus. If a stone is present severe pain and ureteral colic may be elicited by such palpation. It is possible also if the stone is very soft that such manipulation may cause it to disintegrate, following which, the pain will disappear and the patient will pass some sandy sediment with the next urination.

This condition must be differentiated from other causes of acute pain in the lower abdomen and lumbar region, especially those associated with slight fever and leucocytosis, particularly, ruptured ectopic pregnancy, twisted ovarian cyst, acute appendicitis and peripheral neuritis. Pyelitis of pregnancy without stone is usually associated with much less pain and of a less colicky nature. Red cells are much less conspicuous in the urine. The onset is slower as a rule. X-ray will help to differentiate and the passage of a wax-tipped catheter if necessary will demonstrate the position of the stone if present in most cases.

The prophylactic treatment of kidney stone is important. All patients known to have pyelitis during childhood should be thoroughly treated until the urine remains negative for organisms and pus cells. This reduces the chances of stone formation. If a patient who is known to have a kidney stone becomes pregnant an immediate estimate should be made of her kidney functional capacity. This can be judged by the results of various tests such as the phenolsulfonphthalein and Mosenthal tests. Microscopic examination and estimation of the amount of albumin excreted help to determine the amount of damage being done to the kidneys and what effect the irritation thus produced may be having in predisposing to the development of a late toxemia of pregnancy. If slight or no signs of irritation of the kidney parenchyma appear, the pregnancy may proceed without special treatment until evidences of kidney damage are noted.

If the kidney stone is too large to leave the pelvis and engage in the ureter, and is not producing symptoms, it should be disregarded during the pregnancy. Following the birth of the baby it can be removed surgically as soon as the baby is sufficiently developed to offer no feeding problem, usually after four to six months.

A small stone traveling down the ureter should be treated conservatively, in the hope that the ureter may be able to expel it into the bladder from whence it may

he crushed and removed easily through an operating cystoscope. If the stone lodges in the ureter and will not pass, injections of oil may help to dislodge it and permit passage. The tendency of these stones to lodge in the lower end of the ureter in most cases facilitates their removal by this method.

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conclusion was sought through a biologic assay of vasoconstrictor substances in the blood of patients with normal blood pressures, the blood of hypertensive patients and the blood of patients made transiently hypertensive by intravenous injections of angiotonin. Previous studies on the same subject, in the opinion of the authors, have failed to demonstrate conclusively the presence of an excessive amount of pressor substance in the blood of hypertensive patients.

The present investigation was carried out on ultrafiltrates of citrated plasma from five patients with normal blood pressure, nine patients with hypertension and eight patients whose blood pressure had been raised by intravenous injection of angiotonin. It was found that ultrafiltrates of blood plasma from normal and hypertensive patients contain an almost identical amount of vasoconstrictor substance or substances. Ultrafiltrates of blood plasma from patients made transiently hypertensive by angiotonin contain a much greater amount of vasoconstrictor substance than ultrafiltrates of plasma from hypertensive patients whose blood pressures are much higher. The conclusion is reached that angiotonin is not present in increased amounts in the blood of patients with essential hypertension of long duration and that essential hypertension is probably not caused by an increased production of angiotonin.

## A CASE OF RETROPERITONEAL HAEMORRHAGE CAUSING DEATH IN LATE PREGNANCY

MEAVE KENNY AND I. DONIACH

J. Obst. & Gynaec. Brit. Emp., 52: 259-61, 1945

A married woman, 30 years of age, attended the antenatal clinic during the 28th week of her second pregnancy. During her first pregnancy she had been treated for gonorrhoea but no evidence of venereal disease was found now and she appeared very well.

At the 36th week she returned for routine inspection and was found to have edema of the legs. The blood pressure was 160/100 mm. Hg. On the following morning she was brought in unconscious, ashen and pulseless and died within a half hour. At death, a cesarean section was performed and a new-born, mature child delivered. The laparotomy revealed a massive retroperitoneal hemorrhage on the left side.

It was concluded from the husband's disclosure that coitus may well have played the part of precipitating the hemorrhage.

Post-mortem examination showed that the pre-eclamptic clinical signs of hypertension and edema were based upon pathological changes, typical of eclampsia, in the heart, liver and kidneys. The brain, respiratory system, thyroid, adrenals, pancreas and vertebral bone-marrow all were free of gross lesion. The source of the hemorrhage was not discovered. 7 references. 6 figures.

## FATAL HEMORRHAGE FROM AN ANGIOMATOUS POLYP OF ILEUM COMPLICATING PREGNANCY

S. H. POLAYES AND THOMAS F. NEVINS

Am. J. Obst. & Gynec., 50: 207-212, 1945

Approximately 93 cases of angioma of the gastrointestinal tract have been reported in the literature. Only about 13 of these involved the ileum, and in most of these the angioma was one of several lesions coexisting in other segments of the intestines. The present case not only represents one of the few instances in which the lesion was solitary and limited to the ileum but is unique in that the lesion complicated pregnancy.

The patient was a 26-year-old white woman in the sixth month of pregnancy on admittance to hospital for treatment of severe secondary anemia which resulted from repeated attacks of rectal bleeding. The bleeding episodes dated from about six months after a pregnancy resulting in a full-term stillbirth and about 14 months prior to onset of the present pregnancy. The night after admittance to hospital the fetal heart beats stopped and before a blood transfusion could be given the patient died following a massive hemorrhage per rectum. Autopsy revealed no pathologic conditions other than a soft polypoid structure on the ileum, about 50 cm. above the ileocecal junction, covered with fresh blood clot, and an area of superficial ulceration in the mucosa around it. It is suggested that had the diagnosis been made earlier in her course, surgical intervention might have spared the patient's life.

## A QUADRIOVULAR QUADRUPLLET PREGNANCY

B. P. WATSON

Am. J. Obst. & Gynec., 50: 184-190, 1945

This paper reports the first birth of quadruplets in New York City. The birth weights were as follows: Baby A, female, five pounds; baby B, male, five pounds; baby C, female, four pounds twelve ounces; and baby D, female, four pounds thirteen ounces. Examination of the placenta and membranes indicated that each was developed from a separate ovum. At the age of seven months they had no striking resemblances and could easily be distinguished from one another.

## THE TREATMENT OF MYOMAS IN PREGNANCY WHICH ARE UNDERGOING DEGENERATION

H. W. JOHNSTON

Canad. M. A. J., 53: 366-67, 1945

Ten cases of myoma undergoing severe degeneration in pregnancy are presented. The author believes that conservative treatment of such cases is amply justified because of the risk involved for both mother and fetus in the operation of myomectomy on the pregnant uterus.

The commonest type of tumor is a red degeneration or a necrobiosis. The tumor becomes enlarged, tender and painful and fever supervenes. The treatment for all of the ten cases presented in this report was expectant, consisting of rest in bed, heat to the abdomen, sedation and assurance. Five of the patients were delivered by natural channels. Three were afebrile during the puerperium and one had a moderately severe post-partum hemorrhage. Myomas which have undergone degeneration in pregnancy frequently have adherent omentum which may be torn during labor if the tumor is pressed upon. This would result in serious intra-peritoneal bleeding and require immediate laparotomy. The other five of the ten cases were treated by cesarean section at term with myomectomy. Myomectomy is an easy operation in the pregnant uterus. Degenerated or degenerating tumors shell out like peas from a pod.

Since any operative interference with the tumor during the prenatal period, apart from hysterectomy, will probably lead to a misarrriage, it appears wiser to give conservative expectant treatment throughout the pregnancy.

## A CASE OF INCARCERATED UTERUS SUCCESSFULLY TREATED IN 1808

HERBERT THOMS

Connecticut M. J., 9: 771-72, 1945

The author presents an account of a case of incarcerated uterus which was written by an unknown author. The case was treated in 1808 and is interesting partly because of its early record and also because of the method used in its successful treatment.

A 40-year-old woman, pregnant supposedly about three months, in jumping from a horse, felt something give way in her pelvis. The shock was followed by weakness, dysuria, nausea and vomiting. Bimanual pelvic examination, performed 15 days later, revealed a tumor between the rectum and vagina which appeared to be a sack of the rectum filled with indurated feces, the sack having been formed by pressure of the superincumbent uterus. A little farther up the rectum was entirely obstructed by the fundus of the uterus.

No effects were achieved by manual trials to replace the uterus, either with the patient on her back or in the knee-chest position. It was finally restored "by an instrument resembling a probang, made of a cylinder, the size of the finger, and eight or ten inches in length, on the end of which a head was formed, by winding flax and covering it with soft leather, as large as could be passed into the rectum." With the patient on her knees, the chest lower than the pelvis, this instrument was introduced into the rectum. By applying much force both with the instrument and with two fingers in the vagina, the uterus was raised above the brim of the pelvis. After the usual gestation period, the patient was delivered of a healthy child.

## THE PREGNANCY ANEMIAS IN THE LIGHT OF THE STERNAL PUNCTURE

S. THADDEA

Geburtshilfe und Frauenheilkunde 6: 201, 1944

Hitherto existing findings in the bone marrow of pregnant women indicate that the sternal marrow is very rich in cells. Sternal puncture in normal pregnancy shows, as characteristic landmarks, the presence of macroblasts, anisocytosis of promyelocytes, eosinophilia, and plasmacellular reaction of the reticulum cells. These changes are termed "pregnancy reaction of the bone marrow".

True anemias of pregnancy are divided into hypo- and hyper-chromic types. Essential hypochromic anemia of pregnancy is based on lack of iron, as proved by physiologic investigations on the plasma iron chemism. The bone marrow in this condition is hyperplastic as a rule. Particularly the macroblasts are numerically increased. In the sternal marrow there is marked increase of erythroblasts, due either to an excess of immature macroblasts or small normoblasts. Essential hypochromic anemia of pregnancy, after being treated with iron, often shows a "stabkernige" leukopoesis with moderate leukocytosis.

Pernicious anemia of pregnancy is a rare complication of pregnancy. It is differentiated from Biermer anemia by normality of the serum bilirubin level, by normal conditions of gastric secretion, by absence of urobilinogen in the urine, by absence of recurrences outside pregnancy and by the fact that permanent cure takes place following puerperium. Pathogenetically, increased consumption of the antipernicious principle as a result of surplus fetal demand is one of the causes of pernicious anemia of pregnancy. In the sternal marrow megaloblasts and giant "stabkernige" are found.

In pseudopernicious anemia of pregnancy the sternal puncture reveals the same picture of the bone marrow as is seen in normal pregnancy, namely macroblastosis without giant forms of myelopoiesis. As to the "tropical macrocytic anemia of pregnancy", no findings of the sternal marrow exist for the time being. In the presence of the so-called pernicious-like hemolytic anemia of pregnancy asso-

ciated with chronic malaria, megaloblasts are said to occur in the bone marrow. This occurrence is probably due to the fact that the chronic malaria has exerted a noxious effect on bone marrow and spleen.

## THE INFLUENCE OF PREGNANCY ON OTOSCLEROSIS

RICHARD T. BARTON

New Eng. J. of Med., 233: 433-6, 1945

Otosclerosis is a pathologic process of unknown etiology, wherein new spongy bone is formed about the stapes and oval window, resulting in progressive deafness. This process is frequently affected unfavorably by pregnancy, as well as by other endocrine crises. The loss of auditory function may occur at any time in relation to pregnancy—during or after it, or six months or so after parturition.

The relation of pregnancy to this condition, the indication for abortion and the effect of abortion on the progress of the disease have, according to the author, rarely been discussed in English medical literature. However, in Europe the literature in the last decade has been stimulated by German attempts to lay down rules for their eugenics courts to regulate this disease.

Dr. Ruth P. Guildler, of the Winthrop Foundation, made a study at the Massachusetts Eye and Ear Infirmary, of 133 otosclerotic women who had experienced one or more pregnancies. All these cases were examined and tested to make the diagnosis reasonably certain. There were 19 cases in which, for various reasons, it was impossible to ascertain complete information regarding the effect of pregnancies. The results demonstrated that nearly two-thirds of the cases studied were made worse by at least one of their pregnancies (73 cases). Forty showed no appreciable alteration in the course of the disease. In only one case did the hearing improve during pregnancy and this was only temporary. It was the patient's first pregnancy and the hearing returned to the previous level after parturition. This same phenomenon has been observed by other authors.

Many authors have blamed the progression of the disease on certain endocrine changes, those taking place in one of the following periods having been suspected: during pregnancy; immediately after it (during lactation); and six months or more after parturition. In the 73 cases in the series it was demonstrated that the hearing loss commenced immediately after delivery in about half the cases (30 cases); during pregnancy in 12 cases; six months or more after parturition, in 17 of the patients. Whether the increase in deafness in the last group should be attributed to pregnancy or to some other inciting agent is open to question.

The fact that deafness is sometimes made worse by pregnancy does not mean that the hearing loss is always precipitated by the first gestation. One authority states that the damage sustained in the first pregnancy in most cases recedes, whereas that aggravated by later pregnancies usually persists. However, among

51 cases in the present series in which deafness had its onset with the first pregnancy, the damage receded in only two. In all others the hearing loss was maintained. The hearing may or may not be further affected by subsequent pregnancies.

Some writers are of the opinion that aggravation of hearing loss usually occurs not in the first pregnancy but in a later one, and that this is especially true in rapidly successive childbearing. The author of this article states that the present study did not corroborate this, but indicated that the onset of the ear affection occurs most frequently at the time of the first pregnancy. There was little evidence that rapid succession of pregnancies was any more harmful to the hearing than widely distributed gestations. Seventy-two per cent of the patients in this series suffered hearing loss with the first pregnancy and fifty per cent with subsequent ones.

The problem of therapeutic abortion in the management of otosclerosis is an extremely difficult one, and there is great diversity of opinion on the subject. The author believes that abortion is never justified in these cases for the following reasons: the effect of pregnancy on otosclerosis is variable and unpredictable; the favorable effect of abortion on the otosclerosis is inconstant and the progression of the deafness with pregnancy may or may not be arrested by it; the disease does not endanger the life of the mother as do the accepted indications for therapeutic abortion; and this type of deafness is not the severe handicap that it once was, owing to the modern hearing aid and the promise of surgical treatment. Sterilization or other eugenic measures are futile in the control of otosclerosis because the hereditary nature of the disease is not known accurately.

## EFFECT OF RIGID SODIUM RESTRICTION ON BLOOD PRESSURE AND SURVIVAL OF HYPERTENSIVE RATS

A. GROLLMAN AND T. R. HARRISON

Proc. Soc. Exper. Biol. & Med., 60: 52-55, 1945

Observations by the authors during their course of studies on experimental hypertension in the rat have shown that the addition of sodium chloride in very excessive amounts to the normal diet raised the blood pressure only slightly. However, when diets naturally low in sodium chloride were administered without the addition of salt mixture, prompt reduction of the blood pressure occurred to relatively normal levels. The present paper discusses the effect of experimental rigid sodium restriction on rats.

Drastic sodium restriction was shown to result in a marked drop in the blood pressure of rats with experimental hypertension. It appeared that even 0.5 per cent sodium chloride partially prevents the hypotensive effect of a low-sodium diet and that 2 per cent sodium chloride completely inhibits the effect. It ap-

peared that deficiency of sodium rather than of chloride is related to the observed hypotensive effect.

Experimentation on the effect on survival indicated that the decline in blood pressure associated with a low-sodium diet is not only not detrimental to animals with experimentally induced hypertension but appears to be beneficial insofar as duration of life is concerned.

The hypotensive effect in animals on a low-sodium diet was inhibited by the administration of large doses of choline. This inhibitory effect may possibly be due to the pharmacodynamic action of choline in such large doses.

The authors believe it most likely that when subjected to a drastic sodium restriction, the animal with experimental renal hypertension and certain (but not all) patients with hypertension rid themselves of the plethora of salt and water in their tissues and that this secondarily results in the observed reduction in blood pressure.

(Whether this experimental evidence has any relationship with the behavior of sodium in pre-eclampsia cannot be said, but it is in keeping with common clinical experience in that condition. Certainly there is no therapeutic procedure of greater value in pre-eclampsia than the withdrawal of sodium chloride; and even in normal gravidæ it is desirable, as a prophylactic measure, to restrict salt intake in the last month or so.—Ed.)

## SURGICAL EMERGENCIES OF THE ABDOMEN COMPLICATING PREGNANCY

RODNEY L. STEDGE AND JOSEPH L. WILSON

Guthrie Clin. Bull., 15: 59-65, 1945

Forty-three cases of pregnancy complicated by acute abdominal conditions requiring operation at the Robert Packer Hospital since 1927 are reported. This series does not include ectopic pregnancies and cases in which hysterectomies were performed. Appendicitis was the most common indication for operation in this group; 28 appendectomies were performed. These cases were subdivided as follows: acute gangrenous, perforated, 3 cases; acute gangrenous, non-perforated, 3; acute appendicitis, 13; subacute or chronic, 9. An analysis of the appendectomy cases showed a decreased incidence but an increased severity of the attacks during the later months of pregnancy. A high percentage of these patients gave a history of attacks prior to pregnancy. The difficulties in diagnosing appendicitis during pregnancy are discussed and right upper pain due to the upward displacement of the appendix out of the pelvis as pregnancy advances is stressed as a symptom. Muscle spasm is often absent because the abdominal wall is thin and tense. Pelvic or rectal examination is usually non-contributory because of the presenting part and the elevation of the appendix. The maternal mortality from perforated appendicitis approaches 50 per cent and that of the fetus 75 per

cent, as calculated from the authors' material and other reports from the literature. In cases not complicated by perforation or peritonitis, the maternal mortality is about that of the non-pregnant woman and the fetal mortality approaches 10 per cent. The treatment of appendicitis during pregnancy is prompt surgical intervention, without interruption of the pregnancy.

The next most frequent complication requiring surgery was ovarian cysts (9 cases). There were no maternal nor fetal deaths in this group. Five pregnancies progressed to term; the final outcome of the others is not known. Cholecystectomy was performed in one instance. This patient was two-months pregnant and aborted four days after the operation. Myomectomy was performed in three cases. Strangulated hernia was an acute emergency in one case and repair of a traumatic ruptured duodenum was performed in another. There were no maternal nor fetal deaths in these last three groups.

## PATHOLOGY OF LABOR AND PUERPERIUM

### THE INFLUENCE OF MINOR DEGREES OF FAILURE OF FUSION OF THE MÜLLERIAN DUCTS ON PREGNANCY AND LABOR

STANLEY WAY

J. Obst. & Gynaec. Brit. Emp., 52: 325-33, 1945

Occasionally failure of fusion of the Müllerian ducts occurs in humans and may be of varying degree, although most commonly it is slight. The author shows that the congenital defects resulting from this failure of fusion have effects which are little known and serious for both mother and child. He classifies the deformities as follows: (1) Uterus arcuatus; (2) Uterus bicornis unicorpus unicollis; (3) Uterus bicornis unicollis; (4) Uterus bicornis bicornis; (5) Uterus subseptus; and (6) Uterus septus.

Types 1, 2 and 5 are regarded as minor deformities, probably much commoner than generally is imagined. The remaining types are more severe and very much rarer. Since types 2 and 5, although minor, produce abnormalities in pregnancy and labor, their recognition is of importance.

A total of 18 cases having abnormalities of the uterus are presented and described in some detail. The histories of many of these cases show numerous previous abortions. The mode of delivery was most commonly cesarean section. Several children died and one was born with a hair-lip and spina bifida. The maternal deformity most commonly seen in these cases was uterus bicornis unicorpus unicollis.

An attempt was made to radiograph the uteri of several female children. This procedure was abandoned when it proved very difficult and not without danger. The two surviving children in one case were radiographed, one showing a uterine deformity and the other being normal. Another patient with uterus bicornis unicorpus unicollis was delivered of a female child which died on the 4th day of life. Autopsy showed the same deformity present in the infant.

Twelve of the patients had a total of 33 pregnancies of which the details are known and the following complications occurred, in order of their frequency: transverse lie; abortion; breech; premature labor; retention of whole or part of the placenta; prolapsed cord; and placenta previa. Of the 22 viable children delivered, 4 were stillborn, 1 died after breech delivery and 2 died of causes not connected with the uterine deformity. This gives a fetal mortality of 22.8 per cent due to the uterine abnormality.

The author believes that operative correction is indicated where a deformity is definitely known to be the cause of a repeated abortion syndrome, but the risk of rupture of a scar in a subsequent labor must be borne in mind. Patients suffering from the repeated abortion syndrome and those who have unexplained transverse presentations should be subjected to radiological investigation of the uterine cavity so that appropriate measures may be taken to deal with the dangers and

difficulties which may arise in cases of deformities. For the patient who is known to have such a deformity, careful ante-natal care and hospital delivery are essential. The practitioner should bear in mind the fact that daughters of such patients may inherit the deformity. 4 figures. 1 reference.

(The standard anatomical classification of the bicornuate uterus, with its dozen or so subdivisions and its long Latin names, is avowedly cumbersome and lacks, moreover, clinical correlation. From a practical viewpoint it would be much better in Way's opinion to regard all these cases as falling into two main categories. In one group he would place all cases with two uterine cavities. These are gross deformities, are rather rare and behave in a fairly well-established and characteristic manner,—that is, while many patients in this class do very satisfactorily in pregnancy and labor, the incidence of abortion, uterine inertia and retained placenta is high, and occasionally the non-pregnant horn may block the birth canal. In the other category, he would put all cases with one uterine cavity; it is characteristic of these cases that there is a partial septum hugging into the single cavity and it is this septum which causes the clinical difficulties which ensue. These are habitual late abortion, repeated malpresentation, and placental retention.

Way has done a real service, from a number of viewpoints, in directing attention to this latter group of cases which result from minor degrees of failed fusion of the müllerian ducts. In the first place, he cites convincing evidence that the condition is more common than generally realized. Indeed, between the time he submitted the manuscript for publication and the date of its going to press, he was able to add 6 cases to his original 12! In the second place, the many repeated transverse and breech positions in his series attest beyond question the effect—understandable enough—of these septa on fetal position. In this connection it should be noted that Nandy in his excellent study on "Habitual Breech Presentation" has indicated the importance of uterine septa in the etiology of that abnormality (Calcutta M. J., 31: 289-298, 1936). Finally, the author's observations on the hereditary aspects of these malformed uteri are rather startling. As he points out, however, more investigation is needed on this question.

All in all, this is noteworthy contribution and should cause obstetricians everywhere to bear in mind the possibility of these septa when dealing with late habitual abortion, repeated malpresentations and placental retention.—Ed.)

## THE BEHAVIOR OF THE FOETUS IN UTERO WITH SPECIAL REFERENCE TO THE INCIDENCE OF BREECH PRESENTATION AT TERM

C. KEITH VARTAN

J. Obst. & Gynaec. Brit. Emp., 52: 417-434, 1945

This paper is a sequel to one published by the author in 1940 (Lancet, Part I, 595, 1940) in which the theme was advanced that the cause of breech presentation should be sought in those conditions which prevent spontaneous version from taking place. Since this contention is tantamount to saying that breech presentation is very common in mid-pregnancy and that correction of it by spontaneous cephalic version is the rule, the author now presents figures by which hypotheses can be checked.

Careful abdominal palpation was carried out on a consecutive series of ante-

natal patients from the 30th week on ward until such a time as a diagnosis of breech presentation had been made on 1000 patients. If the diagnosis was in doubt, x-ray films were made. This task took three and a half years and the examination of 3875 patients for its completion. On the basis of his observations, the author has drawn up nine postulates, as follows:

1. The incidence of breech presentation at the 30th week is high. Since 1000 breech presentations were observed after only 3875 patients had been examined, it follows that 1 woman in every 4 in this series was known to have a breech at some time or other. Ryder's comparable ratio, based on an analysis of 1721 cases was 1 in 6 (*Am. J. Obst. & Gynec.*, 45: 1004, 1943).

2. In most breech cases spontaneous version takes place. Thus, in the 1000 cases studied this movement occurred 680 times. In 28 of these cases it took place after failed external version.

3. Spontaneous cephalic version is a maneuver which tends to take place once and only once. It occurred only 5 times in this series.

4. Spontaneous cephalic version is only rarely followed by reversion. It was observed only 25 times, a finding at variance with the belief that the fetus is constantly traveling around in the amniotic sac. This suggests to the author that in spontaneous cephalic version the fetus has made a purposive movement, for some definite reason.

5. Spontaneous cephalic version takes place at a specific time in pregnancy. In the present series the bulk of the versions were known to have taken place by the 34th week. Among those cases in which the time was known by which version had taken place, namely, 559, 480 or 85.9 per cent seem to have occurred between the 30th and 34th week, inclusive. The most common time was the 32nd week with the 31st and 33rd weeks next.

6. Spontaneous podalic version is not common. It was observed 134 times in this series of 3875 patients or in 3.46 per cent. If then the fetus reaches the 31st to 33rd week as a vertex, the chance of this presentation being disturbed is remote.

7. External version has a higher reversion rate than has spontaneous version. Indeed, in the present series most of the 134 cases of spontaneous podalic version noted above occurred after one or more external cephalic versions, and the total reversion rate was 21.8 per cent.

8. Failed version is associated with certain definite clinical findings, namely a diminished amount of amniotic fluid or extended legs. Failure to turn the breech to a vertex occurred on 77 occasions. The failure was subsequently overcome, spontaneously 28 times and by the obstetrician 13 times. In the remaining 36 instances the patient was delivered as a breech. X-ray films on these cases of failed version revealed that the attitude of the fetus was regularly one of extension often with an upright stance. The latter indicates a tight application of the uterus to the fetus and means that the quantity of liquor is small.

9. Breech presentation at term cannot be eliminated because of failed external version, spontaneous podalic version, twins, etc. In the present series, of the original 3875 cases, 85 or 2.2 per cent were delivered as breeches. Had only single pregnancies been included, the figure would have been about 1.8 per cent.

(Of the several reasons which have been advanced to explain why the baby at term usually presents by the vertex, about the only tenable one seems to be the pyriform shape of the uterus. Although the measurement of the fetal head at term is slightly larger than the breech, the entire podalic pole of the fetus, that is, the breech plus its flexed extremities, is bulkier than the cephalic pole and more motile; the cephalic pole is represented by the head only, since the upper extremities are some distance removed and are small and less protruding. Until about the 32nd week the mass of amniotic fluid is large in relation to fetal mass and there is no crowding of the fetus by the uterine walls. At approximately this time, however, the ratio between amniotic fluid mass and fetal mass alters in the direction of a relative diminution in amniotic fluid. This brings the uterine walls in closer apposition to the fetal parts and it is only then that the pyriform shape of the uterus exerts its effect; the fetus, if it has been presenting by the breech, changes its polarity in order to make use of the roomier fundus for its bulkier and more motile podalic pole. The high incidence of breech presentation in hydrocephalic fetuses is in keeping with this theory since here the cephalic pole is definitely larger than the podalic. Nor is the high frequency of breech presentations in anencephalic monsters an argument against it since such fetuses are usually premature at delivery and hydramnios is the rule.

As Vartan points out, the cause of breech presentation must be some circumstance which prevents the physiological mechanism described above from taking place. Obviously, abnormal uterine shape can play a rôle in rare cases only, for instance, in cases in which a septum bulges into the upper segment; otherwise, breech presentations would repeat themselves much more often than they do. Vartan believes that some peculiarity of fetal attitude may prevent the fetus from turning itself, particularly extension of the vertebral column in frank breeches; and his series of skiagrams of cases in which the baby did not turn and could not be turned, afford convincing evidence of his contention. Another important factor, he points out, is a diminished amount of amniotic fluid.

Studies such as this have an important bearing on the pros and cons of external version. Some 75 per cent of infants which present by the breech at the sixth month change spontaneously to vertex presentations by term. In the remainder, some special circumstance, presumably an extended fetal attitude or a tendency to oligohydramnios, not only prevents spontaneous version but also makes external version difficult or impossible. This fact explains perhaps why the proponents of external version have been unable to reduce their final incidence of breech presentation greatly below the usual frequency of 3 per cent. Thus, Ryder (*M. Record*, 157: 157-601, 1944) reports 2.7 per cent and the present author, a figure between 1 and 2 per cent, depending on the method of calculation.—Ed.)

## PENICILLIN TREATMENT OF ACUTE PUERPERAL MASTITIS

C. P. HODGKINSON AND R. E. NELSON

J. A. M. A., 129: 269-70, 1945

The authors present cases of twenty-four patients suffering from acute puerperal mastitis who were treated with penicillin. All of these cases resolved without abscess formation.

Bacteriologic studies have shown that most acute puerperal breast infections are staphylococcal in origin. Staphylococci are among the organisms found to be particularly susceptible to penicillin. Sulfonamide therapy has apparently failed to achieve the expected clinical improvement because of the relative ineffectiveness of such drugs on staphylococcal infections.

The clinical course of acute mastitis is characterized by a short period of cellulitis followed promptly by abscess or resolution. Once an abscess has formed, penicillin will not replace adequate incision and drainage. Limiting breast infections to the cellulitis stage must involve early initiation of treatment.

Each of the twenty-four patients in this series received 840,000 Oxford units of penicillin under a five day plan consisting of 25,000 Oxford units every three hours for seventy-two hours, then 15,000 Oxford units every three hours for forty-eight hours. If the breasts were lactating, inhibition was facilitated by using diethylstilbestrol in doses of 5 mg. three times daily until 40 mg. had been given. All patients were discharged between the fifth and eighth days. Abscess formation was prevented in all cases. Recurrence of symptoms failed to develop in any case. 7 references.

## THE DIAGNOSIS OF CEPHALOPELVIC DISPROPORTION

W. T. McCONNELL

Kentucky M. J., 43: 303-07, 1945

The author presents a method for the diagnosis of cephalopelvic disproportion which has proved successful in private and clinical practices.

It is apparent that there are two main difficulties causing preventable deaths of many babies; one of these is undetected cephalopelvic disproportion of the fetus and the other is the case of breech presentation. The author finds that external pelvic measurements are not reliable in determining whether or not a disproportion exists. The factors encountered which make them unreliable are: (1) marked variations in the thickness of the bones forming the pelvic girdle which may mean variations in the internal pelvic capacity; and (2) marked variations in the angle of the iliac bones in relation to the long axis of the birth canal. It is not so much a matter of the external measurement, the size of the baby or even the exact size of the true pelvis, but the relationship between the size of a given head to a given pelvic capacity at the time of birth.

The author's formula for use in cephalic presentations requires measurements from two x-ray views—anteroposterior and lateral of the mother's pelvis. In reading the films, diameters must be accurately measured. The longest diameter of the fetal head is subtracted from the longest diameter of the transverse diameter of the pelvis. Then, from the lateral view, the longest diameter of the head is subtracted from the measurement of the true conjugate of the pelvis from the inside of the symphysis to the promontory of the sacrum. The two differences are added and the sum divided by 2, the result being the total clearance. A total clearance of 1.5 cm. is safe for the baby to be born. One cm. is considered borderline, .5 cm. total clearance is very questionable and minus 1.0 cm. is considered absolute cephalopelvic disproportion.

In this manner all cases may be divided into 3 classes: (1) those in which there

is known to be no cephalopelvic disproportion; (2) those falling into the borderline group; and (3) those which are considered to be absolute disproportion. All patients in class 1 may be delivered from below and all class 3 patients should be delivered through the abdomen. Borderline cases are delivered as indicated by other factors such as ability of the head to mold, character of pains, ease of cervical dilatation, angle of inlet, shape of sacrum, other pelvic abnormalities and muscles and fat of the birth canal.

Because of magnification it has been difficult to rely upon x-ray views of breech presentations in estimating cephalopelvic disproportion. The author finds that by taking anteroposterior and posteroanterior views of the patient, adding these together and dividing by 2, one has the relative proportion of the head to the pelvis.

## ACUTE INCOMPLETE INVERSION OF THE PUERPERAL UTERUS.

### REPORT OF CASE WITH POSTMORTEM FINDINGS

W. C. THOMAS AND D. E. WARD, JR.

N. Carolina Med. Jour., 6: 515-517, 1945

The subject of this report was an 18-year-old white housewife. Both her mother and a maternal aunt had died during labor but no further details of these deaths could be obtained. The patient's menstrual period had been irregular and the flow scanty since menarche at the age of 14 years. Labor began spontaneously and lasted eleven hours. The position of the baby was right occiput anterior. The second stage of labor was carried out under ether anesthesia and a normal baby was delivered by outlet forceps. The placenta separated spontaneously and was expressed intact fourteen minutes after the delivery of the baby. The total blood loss was estimated to be 500 cc. Ergotrate was administered. The patient reacted from the anesthesia promptly, but vomited several times and passed several clots of blood from the vagina. An hour after delivery she suddenly lapsed into a state of profound shock and died ten minutes later. At postmortem examination four hours later a slight amount of bloody fluid issued from the vaginal orifice but no clots were noted within the vagina. The cervix was in the usual immediate postpartum condition of dilatation. The upper limit of the fundus could not be palpated, but when the abdomen was opened the uterine fundus was found to be completely inverted. The internal viscera were markedly congested with blood. Histological examination of the sections through the entire uterus and vagina demonstrated that the placenta had been attached to the anterior and superior uterine walls. Microscopic study of the tissues of the myometrium revealed no pathological alterations. A diagnosis of acute incomplete inversion of the puerperal uterus and peripheral circulatory collapse was made.

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## HUMAN MILK STUDIES: THE DIET OF LACTATING WOMEN AND THE COLLECTION AND PREPARATION OF FOOD AND HUMAN MILK FOR ANALYSIS

MILDRED KAUCHER, ELSIE Z. MOYER, ET AL.

*Am. J. Dis. Child.*, 70: 142-47, 1945

This paper records the vitamin contents of planned dietaries eaten by a controlled group of women during studies of lactation, and of the composition of human milk from the point of view of physiology. The authors describe also the collection and preparation of foods and milk for analysis.

During their ten day stay in the hospital after parturition, the mothers received known diets and complete collections of food, urine and milk were analyzed to determine vitamin, fat, protein and mineral contents and energy value. The same women were studied under the same comparable control and collection for five day periods during lactation at home. The menus on which the diets were based were typical of menus for obstetrical patients and were composed of simple palatable foods.

The intake of protein averaged 109.5 Gm. daily and was 10 per cent above the recommended allowance for lactating women. The average daily intake of energy was 2,936 calories or 98 per cent of the recommended caloric intake. Total vitamin C intake averaged 125 mg., vitamin A, 1,455 micrograms, carotene, 6,248 micrograms, thiamine, 1.23 mg., nicotinic acid, 16.50 mg. and riboflavin, 3.14 mg. It would be difficult for the lactating mother to receive the recommended amount of riboflavin without a generous allotment of milk. In this group each woman received slightly over a quart of milk daily.

The average values determined for ascorbic acid, thiamine and nicotinic acid were considerably lower than those recommended. This fact emphasizes in part the amounts of these vitamins lost in preparation and cooking.

The mean volume of milk secreted per day by six women was on the first hospital day 39 cc., on the third day 618 cc., on the fifth day 1,022 cc. and on the tenth hospital day 1,316 cc. The mean volume secreted at home by six women during the 75 to 99 day stage of lactation was 820 cc. The women's appetites were completely satisfied by the diets, their body weights were maintained, and subsequent papers in this series demonstrate that their milk contained greater concentrations of some of the vitamins than did the milk of women eating self-chosen diets.

## THE NEWBORN

### HUMAN MILK STUDIES: IMPLICATIONS OF BREAST FEEDING AND THEIR INVESTIGATION

I. G. MACY, H. H. WILLIAMS, ET AL.

Am. J. Dis. Child., 70: 135-41, 1945

This paper provides the background for the presentation of the results of a comprehensive study of the secretion of human milk and the composition of human and bovine milk from the point of view of physiology.

The authors state that "the kind and amount of food consumed by people during infancy, childhood and the reproductive period predetermine in a large measure the future health and strength of the nation." The milk of a healthy mother has long been considered the most perfect food for her infant. On the average, the breast-fed infant enjoys a better chance to live and to have fewer illnesses. Breast feeding also saves time, labor and money in addition to the intangible values such as the emotional relationship between the nursing mother and her child.

There is a definite individual physiologic capacity of the mammary gland, shown both in the quantity of milk which can be produced and in the length of time that lactation persists under normal conditions. Within limits the quantity of milk secreted by a normal breast adjusts itself to demand. The chances for full breast nursing are from 65 to 74 per cent, depending upon the age of the patient, parity and whether the nursing is from alternate or both breasts at each feeding. It is concluded that the suckling stimulus does not in any way increase milk production in the presence of a part time or deficient state.

The quality and quantity of milk secretion may be altered by the following conditions: environmental factors; disease; size and anatomic structure of the mammary gland; heredity; and the emotional make-up of the subject.

The present goals in the feeding of infants are the stimulation of wider use of breast feeding and human milk and the application of nutritional principles to the mother's diet so that she may produce breast milk that is adequate both in quantity and in quality. When breast feeding is contraindicated, the ultimate goal is to provide a formula which is superior to human milk for infants. There is need for a revaluation of both human and bovine milk with respect to all the known nutriments, and this and subsequent series of studies were planned to fill this need in part.

The biotin content of the milk reached an average value of 0.38 micrograms per hundred cc. on the ninth postpartum day. The mean biotin content of mature human milk was 0.80 micrograms for women on known diets and 0.82 micrograms for women on self-chosen diets.

No effect of duration of lactation, volume of milk or season of the year could be noted on the values of any of these three vitamins in human milk.

## HUMAN MILK STUDIES: FREE AND TOTAL THIAMINE CONTENTS OF COLOSTRUM AND MATURE HUMAN MILK

CHARLOTTE E. RODERUCK, H. H. WILLIAMS AND ICIE G. MACY

*Am. J. Dis. Child.*, 70: 162-70, 1945

The authors have recorded total and free thiamine determinations for 60 twenty-four hour collections of milk obtained during the first 10 postpartum days and 90 collections obtained 2 to 10 months postpartum from mothers receiving diets of equal quality and known quantity. Comparable values are given for 187 samples representing complete expressions of the milk secreted in 4 to 8 hours by 65 women during the first year of lactation while they were consuming diets of their own choice.

During the first days of lactation human milk contains little thiamine. The concentration of total thiamine increases throughout the first few weeks of lactation to a value in mature human milk of 14.0 to 14.7 micrograms (4.7 to 4.9 international units) per hundred cc.

Free thiamine in mature milk does not have a constant value but increases gradually during lactation. The mean values found were 6.7 micrograms (2.2 international units) per hundred cc. for women receiving known diets and 4.7 micrograms (1.6 international units) for women eating self-chosen diets.

Diet is the principle determinant of the concentration of thiamine in human milk. The emotional and physical states of the woman also are factors.

## HUMAN MILK STUDIES: FREE AND TOTAL RIBOFLAVIN CONTENTS OF COLOSTRUM AND MATURE HUMAN MILK

CHARLOTTE E. RODERUCK, MARGARET N. CORYELL, ET AL.

*Am. J. Dis. Child.*, 70: 171-75, 1945

Determinations were made of free and total riboflavin in 333 samples of milk collected from 80 women throughout ten months of lactation, beginning with the first day post partum. From these the authors present the following findings.

The concentration of total riboflavin rises rapidly during the first five days of

## HUMAN MILK STUDIES: A SIMPLE TECHNIC FOR THE MANUAL EXPRESSION OF MOTHERS' MILK

VELMA DAVIES

Am. J. Dis. Child., 70: 148-49, 1945

The milk sacs, or temporary resevoirs of the continuously secreted milk lie beneath the areola. Not all of them lie just beneath the skin; therefore, complete emptying of the breast requires gentle pressure on the tissue underlying the entire areola. The author describes a method for the manual expression of milk from the breasts which she has used for fifteen years. It is simple and can be mastered easily by the mother.

The only utensils needed are a sterile cup or beaker with smooth rounded edge, a funnel and a storage container. Hands and breasts should be washed in soapy water and dried with sterile gauze or towel. The breast is supported with four fingers of one hand under it and below the areolar tissue. The thumb is on the areola above the nipple and the cup is held with the other hand, its edge against the lower margin of the areola. Gentle pressure is exerted by the thumb downward against the inside of the cup in strokes continued at a rate of 30 to 50 a minute. The technic causes no pain or tenderness, permits free and rapid expression of milk and allows the milk to flow directly into the bottom of the cup. 2 figures.

## HUMAN MILK STUDIES: NICOTINIC ACID, PANTOTHENIC ACID AND BIOTIN CONTENTS OF COLOSTRUM AND MATURE HUMAN MILK

MARGARET N. CORYELL, MARY E. HARRIS, ET AL.

Am. J. Dis. Child., 70: 150-61, 1945

Nicotinic acid, pantothenic acid and biotin were determined in human milk secreted during the first ten postpartum days and in mature milk obtained as late as the twelfth month of lactation. In the assays for these vitamins, microbiologic procedures were employed.

On the tenth postpartum day the mean nicotinic acid content of the milk was 245 micrograms per hundred cc. In 24 hour collections of mature human milk from women on known diets the average nicotinic acid content was 196 micrograms per hundred cc., and in 4 to 8 hour collections from women on self-chosen diets the average was 176 micrograms.

The average pantothenic acid content of the milk for the tenth postpartum day was 304 micrograms per hundred cc. The mean calcium pantothenate content of mature human milk was 256 micrograms for women on known diets and 242 micrograms for women on self-chosen diets.

The authors found the average concentration of vitamin A in mature milk to be 62 micrograms (267 U.S.P. units) per hundred cc. for the women on known diets and 60 micrograms (258 U.S.P. units) for the women on self-chosen diets. The corresponding concentrations of carotenoids were 24 and 25 micrograms per hundred cc. respectively.

The average concentration of vitamin A was high on the first day of lactation, rose to a maximum on the third day and then decreased to approximately the average concentration in mature milk on the ninth and tenth days. The average concentration on the third day was about 3 times that in mature milk.

The concentration of carotenoids on the first day of lactation was about 10 times that in mature milk. It decreased rapidly and began to level off on the fifth and sixth days. On the tenth day the concentration was still slightly above the average for mature milk. Both vitamin A and carotenoids tended to maintain the same concentrations throughout the period of lactation from the thirtieth to the three-hundredth day after parturition.

## HUMAN MILK STUDIES: COMPARATIVE VALUES OF BOVINE AND HUMAN MILKS IN INFANT FEEDING

J. M. LAWRENCE, B. L. HERRINGTON AND L. A. MAYNARD

Am. J. Dis. Child., 70: 193-99, 1945

Since human milk is preferable to cow's milk but is not always supplied, it would be highly desirable to be able to modify cow's milk to provide a formula more nearly comparable to human milk in composition. The authors present a summary of the most recent studies of the constituents of cow's milk and the factors affecting their concentrations in market milk and compare cow's milk with woman's milk as a basis for infant nutrition.

The vitamin A and carotene contents of cow's milk vary as a result of seasonal changes in the cow's diet. The average of mean values is 33 micrograms of vitamin A and 30 micrograms of carotene per hundred cc.

Exposure of the cow to sunlight is an important cause of variation in the vitamin D content of milk. However, it seems possible to say that normal summer milk may contain from 2 to 4 U.S.P. units per hundred cc. and winter milk perhaps one-fourth of this. Clinical experience demonstrates that under present living conditions neither human milk nor cow's milk can always be relied on to protect babies against rickets.

Most investigators have reported between 2.0 and 2.5 mg. of ascorbic acid per hundred cc. of milk as it is obtained from the cow, but only a small percentage of this is contained in the milk received by the consumer. The vitamin C content of breast milk generally is present in higher concentrations than in cow's milk but it is a matter of safety to provide additional vitamin C for both the breast-fed and the formula-fed baby.

lactation and slowly during the next five days. The concentrations of both free and total riboflavin attain the levels characterizing mature milk by the tenth day. The average value of total riboflavin in mature human milk was 41.3 micrograms per hundred cubic centimeters for women on known diets planned by a dietician, and 35.4 micrograms for women on self-chosen diets. Free riboflavin composed from 43 to 86 per cent of the total riboflavin in mature human milk.

### HUMAN MILK STUDIES: ASCORBIC ACID AND DEHYDROASCORBIC ACID IN COLOSTRUM AND MATURE HUMAN MILK

BERTHA MUNKS, A. ROBINSON, ET AL.

Am. J. Dis. Child., 70: 176-81, 1945

Determinations of vitamin C were made on 329 collections of immature human milk obtained during the first 10 days post partum and mature milk obtained as late as the twelfth month of lactation.

The authors found the oxidized form of ascorbic acid, dehydroascorbic acid, in over 35 per cent of the 68 milk samples analyzed and that it accounted for 14 per cent of the total vitamin C (ascorbic acid plus dehydroascorbic acid) in those samples.

Accurate values for the daily secretion of ascorbic acid in breast milk can be obtained only by analysis of 24 hour collections since there were found to be variations throughout the day and night.

Total vitamin C or ascorbic acid or both were determined on 60 24 hour collections of milk secreted during the first 10 days post partum and on 90 24 hour collections obtained from 10 women during periods of 5 consecutive days at intervals in lactation. Likewise, analyses for total vitamin C only were made on 179 samples from 66 women, each sample representing the secretion during 4 to 8 hours while the women were eating diets of their own choice.

The average total vitamin C for milk collected during the first 10 days post partum was 7.2 mg. per hundred cc., and that for partial and complete daily collections of mature milk was 5.2 mg. per hundred cc.

### HUMAN MILK STUDIES: VITAMIN A AND CAROTENOID CONTENTS OF COLOSTRUM AND MATURE HUMAN MILK

MARJORIE LESHER, J. K. BRODY, ET AL.

Am. J. Dis. Child., 70: 182-92, 1945

Analyses for vitamin A were made on 314 collections of milk from 76 women during various stages of lactation from 24 hours to one year. Twenty-four hour collections were procured from mothers receiving known diets.

Bronchoscopic aspiration of the newborn is a relatively benign procedure when properly performed. Usually complete relief is not obtained for 6 to 8 hours after treatment, indicating that removal of secretions from the larger bronchi allows the smaller terminal branches to drain.

The instrument of choice in these cases is the new improved three millimeter bronchoscope devised by Dr. Simon Jesberg. While offering the same inside diameter, its outside diameter is smaller than the old instrument, thus allowing easy passage through the smallest glottic chink and preventing subsequent laryngeal edema.

## THE TREATMENT OF ASPHYXIA

JOSEPH KREISELMAN

South Med. J., 38: 598-604, 1945

Three methods of resuscitation, one suitable for treatment of asphyxia in the newborn and the other two for performing artificial respiration in the adult, are described.

The routine used for the newborn is as follows. As soon as the cord has been cut the baby is placed in a heated bassinet in a 15° Trendelenberg position. The mouth and pharynx are cleared with an aspirator. If the infant does not breathe spontaneously, or if it is cyanosed or pale, oxygen is given without delay. It is important that oxygen be supplied immediately. If the infant is not breathing, the oxygen is supplied with the resuscitator by placing the mask over the nose and mouth with the airway over the tongue. In order to maintain a clear airway the head is extended and the chin held up. The valve lever on the mask is depressed by hand and held down long enough for the lungs to be inflated. When the lever is released the lungs deflate because of their own elasticity. The time required for inflation and for deflation is two seconds each. There should thus be twelve to fifteen inflations per minute. During this process the face mask is not removed as the expired gas will escape through the mask valve. The spasmodic inspiratory efforts with which the breathing of deeply asphyxiated babies usually begins, should be carefully watched and the inflations synchronized with each effort at inspiration, at the same time continuing the per minute rate. When breathing is established but oxygen is still needed, the face mask with the attached airway is removed and the continuous flow mask is placed over the mouth and nose, with the flow meter set at 4 liters per minute. If oxygen is needed over a period of hours or days, the tent hood is placed over the head and the flow meter set at 4 liters. In profound asphyxia, when the larynx is relaxed, tracheal catheterization may be done. Provision is made for the attachment of a tracheal catheter in place of the face mask. Efforts at resuscitation should always be continued without interruption until the baby breathes spontaneously.

The most important of the B vitamin group in cow's milk is riboflavin.<sup>1</sup> Breast milk contains much less riboflavin than cow's milk, 37 micrograms compared with 200 micrograms per hundred cc.

Mature human milk contains on the average 14 micrograms of thiamine per hundred cc. in contrast to 38 micrograms in cow's milk. Thiamine is noted as one of the vitamins most unstable toward heat in neutral or alkaline solutions. It generally is agreed that part of the thiamine is destroyed in the pasteurization of milk.

Breast milk is much richer in nicotinic acid than cow's milk, containing 183 micrograms in contrast to 85 micrograms in cow's milk per hundred cc.

On the average, human milk contains 246 micrograms of calcium pantothenate per hundred cc. compared with 350 micrograms in cow's milk. Similarly, cow's milk is superior to breast milk in biotin content, containing 3 micrograms per hundred cc. compared with 0.8 microgram for breast milk.

An average has been given of 2 Dam-Glavind units of vitamin K per hundred cc. in cow's milk. Others have found no evidence of this vitamin in milk. Breast milk has been found to average 0.5 Dam-Glavind unit per cc. and the level can be raised to 2 units by feeding vitamin K.

Cow's milk has been found to contain 67 micrograms of pyridoxine per hundred cc. in contrast to only 4 micrograms in human milk.

## ATELECTASIS OF THE NEWBORN

HAROLD OWENS

California & West. Med., 63: 225-26, 1945

The author presents the procedure of bronchoscopic aspiration as an adjunct in the treatment of severe cases of congenital atelectasis due to obstruction of the bronchi by body secretions.

The indication for bronchoscopic intervention is any condition in which there is mechanical obstruction of the trachea or bronchus, not correcting itself spontaneously or with the use of approved conservative therapy, and which appears to be leading to the infant's exhaustion. The author believes it imperative prior to the use of bronchoscopy to rule out the various pathological entities which may resemble congenital atelectasis due to bronchial obstruction. Examples of these are asphyxia, congenital disease of the heart and blood vessels, congenital cystic lung, cerebral trauma, blood dyscrasia, pulmonary infection, diaphragmatic hernia and congenital fetal atelectasis. Twenty-three patients have been bronchoscoped with 8 deaths, representing a mortality of 34.7 per cent. Upon postmortem examination it was found that only 2 of the 8 deaths were caused by true atelectasis.

Newborn atelectasis most commonly occurs in premature patients; in this series of 23 cases, 82.6 per cent were premature.

result of it. It has been indicated that buphthalmos occurs when the exanthem is contracted during the third month. An explanation for the fact that other diseases in early pregnancy do not result in anomalies in the infant is that severe virus infections may kill the fetus and lead to abortion where the milder diseases such as rubella cause only damage to the fetus.

The author points out certain advantages in exposing all girls to rubella before maturity. He also discusses the consideration of abortion of women who have contracted rubella in early pregnancy.

## CON GENITAL CATARACTS FOLLOWING RUBELLA IN PREGNANCY

ARLINGTON C. KRAUSE

Ann. Surg., 122: 1049-1055, 1945

Some of the literature on the effect of rubella in pregnancy is reviewed. In this review 124 cases are cited in which the infants had congenital defects. Of these there were 96 with cataracts, either alone or in addition to other defects. Five new cases of congenital anomalies in infants born to mothers who had had rubella during pregnancy are reported from the University of Chicago. The respective diagnoses were as follows: Case 1, prematurity, congenital heart disease, congenital displacement of the fourth toes and bilateral congenital anterior uveitis and cataracts; Case 2, bilateral fetal uveitis, bilateral congenital cataract, cerebral agenesis and mental retardation not related to blindness; Case 3, spina bifida with loss of function below T 12, congenital cardiac anomalies, congenital cataract of the left eye (this infant died on the 30th day of life); Case 4, congenital cataract, dental aplasia, bilateral total deafness, and mental and physical retardation; Case 5, bilateral congenital cataracts, congenital heart disease, cerebral agenesis and mental retardation. The times of occurrence of rubella during pregnancy were, respectively, seventh week, second month, second month, 2 weeks after last menstrual period, and second month. Preventive measures, such as induction of the disease before pregnancy to those who are exposed to it and therapeutic abortion if the disease occurs in the first four months of pregnancy, and conservative and radical treatment of the infant are discussed.

## ANAEMIAS OF THE NEWBORN

G. B. WISWELL

Canad. M. A. J., 53: 555-61, 1945

Anemia is any state in which the hemoglobin is less than normal in proportion to the blood volume; in the newborn it is a symptom rather than a disease.

When suitable apparatus is not available, the mouth to mouth or mouth to tracheal catheter method, combined with the principles outlined above, may be used. Manual methods in the resuscitation of the newborn are not advised since air cannot be expressed from an airless lung and damage to the viscera and ribs may occur.

## CONGENITAL ANOMALIES FOLLOWING MATERNAL RUBELLA IN EARLY WEEKS OF PREGNANCY, WITH SPECIAL EMPHASIS ON CONGENITAL CATARACT

C. H. ALBAUGH

J. A. M. A., 129: 719-23, 1945

Available data would suggest that 100 per cent of the mothers who contract rubella in the first two months of pregnancy, and approximately 50 per cent of those who contract it during the third month, will give birth to infants with congenital anomalies.

In a series of 78 cases reported by Gregg, a history of rubella was obtained in all but 10 cases and in this latter group the diagnosis was sufficiently suspected for them to be included. All of the infants were found to have cataract at birth, bilaterally in all but 16 cases. In all instances, the nuclear portion of the lens was most affected. Definite congenital heart lesions were reported in 44 of this series. Nearly all the babies were poorly developed and presented feeding problems. Swan and his associates reported the collected data on 61 infants, 36 of which had congenital defects. Thirty-one of the mothers had rubella during pregnancy and gave birth to offspring having congenital defects. Twenty-nine of these mothers had contracted rubella during the first three months of pregnancy. All of the twenty-five who contracted rubella during the first two months gave birth to infants having congenital anomalies but of the eight who contracted the disease during the third month, only four had babies with congenital defects. Among the 31 infants who were congenitally defective, the following abnormalities were noted: (1) 14 children had eye defects (13 had cataract and 1 had buphthalmos); (2) 7 were deaf-mutes; (3) 17 had cardiac defects; (4) 4 were mentally retarded; (5) 1 had hypospadias; and (6) 1 had talipes equinovarus.

The author comments upon Swan's examinations of sections of the lens in which he discovered that the characteristic picture is that of complete necrosis of the nucleus with more or less distortion of the secondary fibers. The critical period for attack upon the lens nucleus would be before the eighth week of pregnancy; the process on the secondary fibers apparently continues to be evident after the seventh and eighth weeks. All the cardiac defects were related to the septums and the ductus arteriosus. It is known that the critical period for the development of cardiac defects is from the fifth to the eighth week.

Other observations and questions are discussed. It has been suggested that these defects are not a new complication of rubella but a previously undetected

result of it. It has been indicated that buphthalmos occurs when the exanthem is contracted during the third month. An explanation for the fact that other diseases in early pregnancy do not result in anomalies in the infant is that severe virus infections may kill the fetus and lead to abortion where the milder diseases such as rubella cause only damage to the fetus.

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Anemia is any state in which the hemoglobin is less than normal in proportion to the blood volume; in the newborn it is a symptom rather than a disease.

Anemia of the newborn is not common but when it occurs it requires immediate treatment. It may be associated with hemorrhage, infection, prematurity and hemolysis.

The problem of the control of hemorrhage due to hypoprothrombinemia has been practically solved by the prophylactic and curative use of vitamin K and as a result there should be no fatalities arising from this cause.

The anemia of infection responds to frequent transfusions while that of prematurity tends to improve spontaneously provided that the nutrition of the infant is good. The author states that iron is not of much value in anemias.

The discovery of the Rh factor and of its relation to the pathogenesis of erythroblastosis has cleared away the mystery of hemolytic disease. Until recent times, 5 per cent of the total fetal mortality was due to erythroblastosis, a greater cause than that of congenital syphilis. The use of Rh negative blood is saving the lives of these infants and has reduced the death rate from 71 to 14 per cent. It is therefore imperative for all maternity hospitals to have Rh negative blood donors available at all times.

## LARGE SCALE TESTING FOR RH NEGATIVE BLOOD

LESLIE H. TISDALL AND DONALD M. GARLAND

*With the Technical Assistance of*

EVAN L. DURHAM

J. A. M. A., 129: 1079-1080, 1945

A swift and easy method of Rh determination perfected by the Army Whole Blood Procurement Service is described. It utilized only the combined serums anti-Rh<sub>0</sub>' containing the two agglutinins Rh<sub>0</sub> and anti-Rh'. Each bottle of blood brought to the laboratory was accompanied with a sample of undiluted blood. The undiluted cell suspension, which remains after the serum in the sample tube has been aspirated, is used for the test. A plate glass slide, 8 by 7 inches ruled off into 1-inch squares, is used for the testing. This permits fifty tests to be run off simultaneously, together with the necessary controls. A drop of anti-Rh<sub>0</sub>' serum at room temperature is placed on each square by means of the dropper supplied with the bottle. A drop of the undiluted cell suspension is then added with a separate medicine dropper for each test. The resulting suspension is then thoroughly mixed by means of the bottom of a Kahn tube and controls with known negative and positive cells are set up. The cell mixtures are allowed to remain on the flat surface for one minute. The slide is then rotated gently from side to side to loosen any cells adherent to the glass. When the positive control shows complete agglutination, the tests are immediately read macroscopically. The setting up and reading of fifty tests can be done in 15 minutes. In order

to check the accuracy of the technique a parallel test was run with the test tube method. A 98 per cent agreement of the results obtained by the two methods was found. The difference is explained by the fact that one serum was of the 85 per cent type while the other was of the 87 per cent type. The finding of 14.2 per cent Rh negative blood in 22,133 tests is in accordance with previously recorded figures. The percentage of Rh negative bloods among 283 Negro bloods which were separately recorded, were also consistent with the results of other investigators.

## AN UNUSUAL CASE OF ERYTHROBLASTOSIS FOETALIS

E. F. AUBERT, J. B. COCHRANE AND M. E. ELLIS

Brit. M. J., 2: 648-49, 1945

The case presented in this report is concluded by the authors to be one of erythroblastosis fetalis due to heterospecific pregnancy (i.e., maternal anti-A or anti-B isoagglutinins).

The patient, a 24-year-old primigravida was found to have a normal pregnancy on her first visit to the antenatal clinic except for an intermediate degree of pelvic contraction. The prenatal course was uneventful and the patient was admitted in labor at the approximate time of confinement. The fetus was in the vertex left occipito-lateral position and the head poorly flexed and mobile; no hydramnios was present. Since no disproportion was present, a trial labor was permitted. After a first stage lasting approximately 22 hours and a second stage of 2 hours, a live mature male infant with gross hydrops fetalis was delivered by manual rotation and forceps. The infant died 25 minutes later.

Necropsy of the infant showed gross edema of all the viscera with much greenish fluid in all the serous cavities. Histological examination of pieces of liver, thymus, spleen, sternum and a lymph node showed the characteristic histological picture of erythroblastosis fetalis.

Serological studies revealed the father's blood to be Group A Rh-negative, the mother's blood to be Group B Rh-negative and the fetal blood to be Group A Rh-negative. The mother's anti-A titre was 16,000,000. Anti-A was found present to a titre of 128 in a sample of fetal cord blood. The father's cells were agglutinated to a titre of 250,000 by the mother's serum. Five weeks after delivery the maternal anti-A titre was 4,000,000. In view of the extraordinarily high maternal anti-A iso-agglutinin titre and of the presence of anti-A in the fetal blood, the authors conclude that this case of erythroblastosis fetalis was due to heterospecific pregnancy.

## THE EFFECT OF THE PREDIABETIC STATE ON THE SURVIVAL OF THE FETUS AND THE BIRTH WEIGHT OF THE NEWBORN INFANT

HERBERT C. MILLER

New England J. Med., 233: 376-78, 1945

One of the outstanding characteristics of infants born to diabetic mothers is a high fetal and neonatal mortality rate. In addition there occur in some of these infants certain somatic and visceral changes among which is an increased birth weight. Since all of the mothers thus far studied have been diabetic during the childbearing period, the author considered it desirable to extend the observations to infants born to mothers whose diabetes appeared after they had passed the fourth decade. The data presented in this report were accumulated from the files of the New Haven Hospital.

It was found that the fetal and neonatal mortality rates and the average birth weight are increased among infants born to mothers who subsequently manifest diabetes mellitus, even though these women do not develop the disease until after forty years of age. In a comparison of infant mortality rates, the rate of 8.3 per cent for a group of prediabetic mothers is significantly higher than the rate of 2.0 per cent for a nondiabetic group. The average birth weight of 112 infants born to 40 nondiabetic mothers was 3.53 kg.; that of 22 infants born to 16 prediabetic mothers was 4.15 kg.; and that of 17 infants who were born 15 years or less before the onset of maternal diabetes was 4.40 kg. The fetal and neonatal mortality rates increase as the onset of maternal diabetes is approached. The author found that maternal obesity is not a factor in the increased birth weight of infants born to prediabetic mothers who became diabetic after the age of forty.

Presumably the primary factors responsible for the increased newborn mortality and increased birthweights of infants born to prediabetic mothers are the same as those that are responsible for such conditions in infants born to mothers who already have developed the disease. Recent studies suggest that fetal and neonatal deaths in diabetic pregnancies are related to a premature increase in estrogen and progesterone production by the placenta, followed by a decreased production of these same steroids at an earlier time in the gestation period than is to be expected. The striking changes in the islands of Langerhans, adrenal glands, gonads and anterior hypophysis of some infants born to diabetic mothers are additional evidence that endocrine factors are involved in their production. The fact that fetal and neonatal deaths are increased for several years before the appearance of diabetes in the mothers points toward a high degree of sensitivity on the part of the human fetus to the factors involved, whether or not they are endocrine. The author states that the fact that all these somatic and visceral changes can be found in the infant several years before there is any evidence of maternal diabetes suggests that additional knowledge of the etiology of diabetes

is to be gained by further study of the factors responsible for the increased mortality rate and the somatic and visceral changes seen in infants born to diabetic mothers.

Data presented in this study indicate a new explanation for the excessive birth weight of some fetuses. The fact that 11 of 12 mothers having babies born to them fifteen years or less before the onset of maternal diabetes were delivered of infants weighing 4 kg. or more suggests that women developing diabetes past the childbearing period are recruited almost wholly from 5 to 7 per cent of mothers who give birth to babies weighing over 4 kg. 6 references.

## THE RH BLOOD FACTOR AMONG TWINS

H. H. STRANDSKOV AND GERTRUDE W. DIEDERICH

Human Biol. 17: 195-206, 1945

The authors are interested in examining the degree of genetic determination of the originally discovered Rh variations and also in testing the mode of inheritance which was suggested for them by Landsteiner and Wiener.

Fifty-three monozygotic or "identical" and 59 dizygotic or "fraternal" pairs of twins were tested for the originally discovered Rh factor. (Tests were not made for the newly discovered subdivisions of the Rh factor.) The two members of the 53 tested monozygotic sets were in every instance of the same Rh type. This perfect concordance among monozygotic twins gives credence to the conclusion that the originally discovered Rh variations are completely determined genetically. The two members of the 59 tested dizygotic sets were both Rh positive in 49 pairs, both Rh negative in 5 pairs and different in 5 pairs. Although these results are not direct evidence for complete genetic determination of Rh variations they agree with expectations based on this conclusion.

The authors compare statistically the observed frequencies of the different Rh combinations among both monozygotic and dizygotic twin pairs with those expected according to the proposed unifactorial mode of inheritance of Landsteiner and Wiener. The agreement between the two sets of data was found to be close. Hence, the authors conclude that the observed frequencies support the proposed mode.

The effect of erythroblastosis on the percentages of Rh combinations expected among twins between the time of conception and high school age was examined. It was found to be negligible and that no correction for it is warranted.

In evaluating the Rh factor as a criterion for the diagnosis of twins, it was shown that about 10 per cent of all white twins and about 7.7 per cent of all same-sex white twins should be diagnosable as dizygotic on the basis of Rh tests alone.

A brief review is made of the occurrence of erythroblastosis in twin pairs in

which one member is Rh positive and the other is Rh negative. The authors estimate that from 10 to 12 such sets of twins should occur annually in the white population of the United States.

## ISO-IMMUNISATION TO THE BLOOD GROUP FACTORS A, B AND RH

K. E. BOORMAN, B. E. DODD AND P. L. MOLLISON

J. Path. & Bact., 57: 157-69, 1945

The object of the authors in the present investigation was to study in greater detail immune responses to the blood group factors A, B and Rh in the human subject following incompatible blood transfusion and pregnancy. As it is now established that hemolytic disease of the fetus is usually due to the presence of immune anti-Rh iso-agglutinins in the mother's serum, the clinical condition of the infant was noted in every case in which such immune iso-agglutinins were produced following pregnancy.

There is in the main a great similarity between the immune responses evoked by the antigens A, B and Rh. In the present study, there was an immune response to the A and B agglutinogens in the majority of instances, namely in 5 out of 5 transfusion cases and in 36 out of 44 pregnancy cases. Anti-Rh agglutinins were usually produced only after repeated transfusions or repeated pregnancies.

In all cases iso-agglutinins are produced which reach a maximum concentration in the serum between the 5th and 20th day after the elimination of the transfused erythrocytes or after delivery. This is true whether the stimulus is provided by an incompatible blood transfusion or by a fetus. In spite of this marked similarity, the authors point out that there are, however, certain differences. While anti-A and anti-B agglutinins occur naturally in the sera of all people whose erythrocytes lack the corresponding agglutinin, anti-Rh agglutinins do not. Consequently there is always a response of the anti-A or anti-B iso-agglutinin after transfusion of incompatible A or B blood, but most Rh-negative individuals do not appear to respond to a first transfusion of Rh-positive blood, although they may produce immune responses after subsequent transfusions. Similarly it may be only after stimulation by several Rh-positive fetuses that the mother acquires an Rh antibody and an infant with hemolytic disease is born.

On the whole, the peak titres of agglutinin in immune anti-A and anti-B sera are higher than the peak titres of anti-Rh sera. On the other hand, the magnitude of the immune response is as great for Rh as for A and B. In the case of the Rh factor and pregnancy, the authors found no direct relationship between the number of stimuli received by the mother and the peak titre attained. Furthermore, there was no obvious relationship between the titre of anti-Rh

iso-agglutinin in the mother's serum and the severity of the disease process in the infant.

## BLOOD GROUPS, SUBGROUPS, M, N TYPES AND RH SUBTYPES IN FILIPINOS

R. T. SIMMONS AND J. J. GRAYDON

M. J. Australia, 2: 325-28, 1945

Blood samples from 382 selected Filipinos, nearly all unrelated adults, have been tested for blood groups, the subgroups of A, the M, N types, and the Rh factor.

The group percentages were group O, 45.0; group A, 22.0; group B, 27.0; group AB, 6.0. Of 107 subjects of blood groups A and AB, the blood of 106 was found to be of subgroups A<sub>1</sub> and A<sub>1</sub>B. The blood of one exception belonged to subgroup A<sub>2</sub>.

The type percentages were: M, 25.9; type MN, 50.3; type N, 23.8.

Of the 382 samples, 381 (99.7%) were found to be Rh-positive.

A method is given for the preparation of a slightly modified Rous and Turner glucose-citrate solution for preserving red cells. Sterile samples of blood stored in the solution at 38°F. for twelve months have been found to be free from hemolysis and to give specific group, type and Rh agglutination.

## HEREDITY OF THE AGGLUTINOGEN RH

PAUL MOUREAU

Am. J. Clin. Path., 15: 405-06, 1945

In a study on the heredity of Rh, 62 families with 128 children have been examined and the findings and conclusions obtained are presented in this report.

There appears to be no doubt that Rh-negative individuals constitute a homozygous recessive type. In families where both parents are Rh-negative, all the children are Rh-negative. It is also established that among Rh-positive individuals, some are homozygous while others are heterozygous.

From the proportion of Rh-positive and Rh-negative children observed in the two sorts of mating in which one or both of the parents are heterozygous it is still impossible to determine whether the heterozygous individuals have a simple genotypic formula corresponding to heredity as a simple unit character or to a complex genotypic formula corresponding to a polygenic inheritance.

The author concludes that one can predict the eventual feasibility of applying the property Rh in tests for the exclusion of paternity.

## CORD TRANSFUSION IN THE MANAGEMENT OF A PREMATURELY DELIVERED INFANT WITH ERYTHROBLASTOSIS FETALIS

CLIFFORD H. HARVILLE

J. A. M. A., 129: 801-02, 1945

With the hope of further reducing the high toll still exacted by erythroblastosis fetalis, premature termination of pregnancy has been advocated in order to limit the period of intra-uterine hemolysis. A neglected procedure which the author believes to be of the greatest value in the management of these prematurely delivered infants is the use of the umbilical vein for the initial blood transfusion. The simplicity of this method and the promptness of blood administration it assures commend it also for the initial transfusion of the full-term infant suspected of having erythroblastosis. The author presents the following case to illustrate the successful use of cord transfusion in conjunction with early delivery in the management of erythroblastosis fetalis.

The patient, quintipara, sextigravida, had a history of 3 normal pregnancies with normal children. The fourth child became deeply jaundiced after birth but recovered. Her fifth pregnancy resulted in the delivery of a full-term jaundiced infant who died on the fourth day. Necropsy findings were those of severe hemolytic disease.

This patient was type AB Rh negative, her husband was type O Rh positive and each of the 4 surviving children was Rh positive. With the obstetrical history and the virtual certainty that the fetus in this pregnancy was Rh positive, premature delivery seemed the most likely means of saving the infant.

A cesarean section was performed 30 days before estimated term, the umbilical cord clamped and 60 cc. of type O Rh negative blood were given to the infant through the umbilical vein. Studies of blood aspirated from the cord vein revealed a hemoglobin content of 8 Gm. per hundred cc., a red blood count of 2,690,000 and only 7 erythroblasts per hundred leucocytes. The infant's blood type was subsequently found to be type O Rh positive.

A second transfusion was given on the second day. The infant improved and at 4½ months its development has been in all respects normal and its weight is that of an infant of the same age born at term.

This case lends support to the thesis that in carefully selected cases of erythroblastosis fetalis early delivery is a rational therapeutic procedure. Cord transfusion is an important adjuvant procedure in the management of the prematurely delivered erythroblastotic infant and also for the initial transfusion of the full-term infant suspected of having this disease.

(Some authorities, notably Diamond and Abelson, are opposed to transfusion in erythroblastosis unless the hemoglobin concentration falls to 7 or 8 gr. per 100 cc. They disapprove of prophylactic transfusion and believe that these infants are better off if they can be pulled through without any transfusion. If it must be done, they prefer to use washed red-cells rather than whole blood. Contrariwise, a number of competent observers would agree with Harville in regard to the value of prophylactic transfusion. Obviously, a larger experience is going to be necessary before this question can be settled.—Ed.)

## PERSISTENCE AND HYPERPLASIA OF THE PRIMARY VITREOUS

ALGERNON B. REESE AND FRANK PAYNE

Am. J. Ophth., 29: 1-24, 1946

Persistence and hyperplasia of the primary vitreous is known more frequently perhaps as "Tunica vasculosa lentis" or "retrolental fibroplasia." It is a condition which usually manifests itself as a bilateral congenital lesion of premature infants, has always appeared sporadically but of late years has shown an increased incidence. Since the disease is particularly prone to develop in very premature infants, the authors attribute its augmented frequency to the increased survival rate of such infants consequent upon modern pediatric care. Fifty cases are reported.

In the authors' opinion the disease results from the fact that the primary or embryonic vitreous, which is interposed between the lens and retina as a vascularized mesoderm, persists in some or all its phases at birth instead of undergoing normal absorption in late prenatal life. This failure of normal involution or disappearance of the primary vitreous is often associated with progressive changes such as actual hyperplasia of the mesoderm, followed by hemorrhage, contracture, swelling of the lens, secondary glaucoma and corneal opacity.

Sixty per cent of the authors' cases were in premature infants. In some instances the abnormality was noted at birth but in others the baby was several months old before the parents realized that the infant was not seeing things.

The authors are inclined to think that the same factor which causes the premature labor in these cases is also responsible for the ophthalmological condition, but after reviewing such possible obstetrical causes as infection and hemorrhage, they are unable to cite a definite etiological factor.

## EYE CONDITIONS AMONG CHILDREN OF PREMATURE, FULL TERM AND HYPERMATURE BIRTH

THOMAS H. EAMES

Am. J. Ophth., 29: 57-63, 1946

One hundred fifty-five children who were born before completion of the normal term of pregnancy or who weighed  $5\frac{1}{2}$  pounds or less at birth are compared with 439 children born at full term or with a birth weight of more than  $5\frac{1}{2}$  pounds. These two groups are compared with a smaller group of children born during or later than the tenth calendar month. The outstanding tendencies noted are the higher frequency of low vision at all of the ages studied among those born prematurely and the poorer median visual acuity through the ninth year in the same group. The presence of somewhat comparable defects and deficiencies in both the premature and hypermature groups provides a suggestion that hypermaturity

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rule, while quite likely the most important in most nurseries, is certainly the most neglected.

## PENICILLIN OINTMENT IN THE TREATMENT OF IMPETIGO NEONATORUM

EDWIN L. KENDIG AND RUSSELL H. FISKE

Jour. Amer. Med. Assoc., 129: 1094-1095, 1945

Fourteen cases of impetigo neonatorum treated with penicillin ointment are reported. The penicillin ointment was freshly prepared each time by taking up a stock solution of penicillin in a eucerite type base (5 per cent by weight) and dispersing in White Ointment U.S.P. XII. For the first cases the ointment was made up with 250 units of penicillin to each gram, but the penicillin was later increased to 333 units to each gram. The exfoliated membrane of epidermis was completely removed by means of alcohol on cotton. The ointment was applied at least twice daily in generous amounts to the moist red base which remained and to the surrounding area of skin. No bath was given until the lesions were completely dry. At the time of discharge from hospital, the mother was instructed to follow the same routine for at least a week, or until no lesions were present. In this series no new lesions appeared after the treatment had been in effect for 48 hours, and after a maximum of three days all the lesions appeared to be dry and healed. In three instances there was a recurrence of the condition after the infant had been home from hospital more than one week, after treatment had been discontinued and baths had been started. Two of these were of only moderate severity and the other was mild.

## TERATOMA OF THE PERINEUM IN A NEWBORN INFANT

A. F. LASH

Am. J. Obst. & Gynec., 50: 344-46, 1945

Embryonic new growths arising at the caudal pole of the embryo are more numerous than those of the cranial pole. They may be situated within the pelvis, anterior to the sacrum and coccyx and behind the rectum; posterior to the bony structures and beneath the skin; or rarely, in the perineal region.

The author presents the case of a female child, weighing 4 pounds, 12 ounces, delivered at the thirty-sixth week of pregnancy. The infant showed normal development except for a red, glistening, smooth, cylindrical mass, about 2.5 cm. long and about 1 cm. in diameter, extending from the perineum just below

may prove to be of similar but probably less importance than is prematurity as an initial handicap.

(This paper may seem a far cry from practical obstetrics but actually the question at issue is of the utmost importance to any physician who delivers a premature infant. One pediatrician has claimed that some 20 per cent of premature babies develop retrolental fibroplasia; and since the condition is associated with varying degrees of blindness, the statement has caused quite a stir among obstetricians, pediatricians and ophthalmologists alike. Fortunately, studies at present under way indicate that the condition is much less common than indicated above.—Ed.)

## PRACTICAL IMPLICATIONS OF THE EPIDEMIOLOGY OF THE DIARRHEAL DISEASES OF THE NEW-BORN

JAMES WATT

Am. J. Pub. Health, 35: 1205-09, 1945

The diarrheal diseases constitute one of the major preventable causes of infant morbidity and mortality. In this report the author discusses the epidemiological features of these diseases with emphasis upon means of prevention.

Although the etiology is only partially known at this time, outbreaks and isolated cases may be divided into four classes: (1) known pathogenic bacteria such as *Shigellae* and *Salmonellae* causing diarrhea; (2) bacteria whose etiological relation is suspected but not known such as *paracolon bacilli*, *pseudomonas*, etc.; (3) virus infections; and (4) parenteral infections.

An outstanding feature of reports on nursery diarrhea is the infrequency with which recognized pathogens have been isolated. One factor contributing to this is the frequency with which some of the usually non-pathogenic organisms are encountered in abnormally large numbers of the stools of sick children.

The recognized pathogens which cause diarrheal disorders escape to the outside only in feces and are spread chiefly by person-to-person contact. The author suggests that these infectious agents enter the nursery in part by doctors, nurses, attendants, mothers and visitors. Also, he stresses the fact that babies themselves should be regarded as potential vectors. Cases are cited of infants who developed diarrhea and whose mothers were found to have diarrheal disorders.

The points which, from the epidemiological point of view, should receive major unrelenting attention are presented. First, the sterility of all supplies should be insured, particularly those which are potential means of mass spread of infection. Second, outside contacts should be limited in so far as possible and all necessary contacts should be assured as safe ones. Third, a technique should be adopted in the nursery which emphasizes the danger of all children as potential sources of infection, regardless of their state of health. The author believes that this latter

material at frequent intervals since the first night after birth. She passed normal meconium twice, then small amounts of fluid with tiny particles of solid yellow stool. Barium was given by mouth in the maternity hospital, but no abnormality was observed. However, X-ray examination made at the Massachusetts General Hospital showed numerous small areas of calcification on the surface of the right lobe of the liver, opaque material in the stomach and one loop of the bowel, and free air scattered throughout the peritoneal cavity. The patient was slightly jaundiced and moderately dehydrated. A diagnosis of meconium peritonitis with intestinal obstruction due to congenital stenosis or atresia was made. The infant died before operation could be performed. At autopsy a congenital diaphragm of the jejunum was found that could have been surgically removed with probable cure of the patient. Surrounding some of the areas of calcification that were seen on the X-ray films were conified epithelial cells and some suggestion of true bone formation. The exact site of perforation could not be demonstrated, but probably occurred in the duodenum close to the right lobe of the liver.

the fourchette. There was no communication with either the vagina or the rectum. On the twelfth postnatal day, the mass was resected and the edges brought together. The wound opened on the sixth postoperative day, but healed satisfactorily by secondary intention. The baby has continued to thrive and develop normally.

The teratoma in this instance was a mixed tumor consisting of derivatives from the entoderm and mesoderm and located in a rarely seen location, the perineum. 2 references. 3 figures.

## CONGENITAL DIAPHRAGMATIC HERNIA WITH DESCRIPTION OF A NEW SIGN

A. SHAFIK ABBASY

Arch. Pediat., 62: 285-8, 1945.

A case is reported in which a diagnosis of diaphragmatic hernia in a five-month-old infant was made by means of the "trumpet sign" before x-ray confirmation. On auscultation in front on the left side a definite medium pitched sound, exactly resembling that of an automobile horn and occupying the whole inspiratory phase with a crescendo note, was heard with each deep inspiration. This sound became weaker or disappeared completely on shallow breathing during sleeping or quiet respiration. It could be easily reproduced when the child was irritated or started to cry, with the result that deep respiration took place, but not when the stomach was full. This sound was also faintly heard on the upper abdomen. The author explains the possible mechanism involved in the production of this sound in that by the descent of the diaphragm during inspiration and the resulting increase of intra-abdominal pressure, the air inside the abdominal portion of the viscus is forced through the comparatively narrow neck of the viscus at the diaphragmatic orifice to its thoracic part. If this explanation is correct, the sign is not to be expected in cases where the defect in the diaphragm allowing the herniation is wide.

## MECONIUM PERITONITIS

ALLAN M. BUTLER, BENJAMIN CASTLEMAN, MILFORD D. SCHULTZ AND  
SIDNEY FARBER

New England J. Med., 233: 257-259, 1945.

This is a discussion of a case record as presented at one of the weekly clinicopathological exercises of the Massachusetts General Hospital. The infant was admitted to hospital at the age of five days because of vomiting of fecal

in certain major complications from another viewpoint, 62.5 per cent of all cases of placenta previa were delivered abdominally, the remainder by other methods; 14.2 per cent of the patients with premature separation of the placenta were delivered abdominally, the remainder by other methods; and 2.7 per cent of the cases of pre-eclampsia were delivered abdominally, the remainder by other methods.

The maternal deaths in the 1887 cases numbered 24, giving a total maternal mortality rate over the 10-year period of 1.3 per cent. During the first five years, it was 1.9 per cent; during the latter five-year period 0.7 per cent. Ten of the deaths were due to peritonitis and 7 to hemorrhage. There was a preponderance of fatalities from peritonitis on the public service, from hemorrhage on the private. The total stillbirth and neonatal death rate, in cases in which the infant was viable, was 6.8 per cent.

(This exhaustive study of cesarean section by one of our acknowledged masters contains so many good texts for obstetrical sermons that it would be difficult to enumerate them all. Particularly instructive from the viewpoint of stressing an important disadvantage of the operation are these facts: among the 1736 cesarean sections done in viable pregnancies, 361 or 20.8 per cent were performed because of previous abdominal delivery and among these 361 patients, 213 or 59.0 per cent underwent sterilization at the time of the operation. I have been in the habit of teaching that there are two hazards associated with cesarean section: (1) the immediate operative danger, and (2) the remote danger represented by the uterine scar and its everlasting threat of rupture in future pregnancies. The immediate danger of the operation has been greatly reduced in recent years as Irving's low maternal mortality rates beautifully attest. However, the remote hazard which abdominal delivery imposes continues to loom almost as large as it ever did; such a patient must look forward very often to another cesarean section, again with its immediate risk, and also, though she usually doesn't know it, to the possible danger which every subsequent pregnancy will impose of uterine rupture. These handicaps were considered sufficiently serious in the present series to call for termination of childbearing in well over half of the cases.

That too many sections are still being done was forcibly brought to my attention recently by an inquiry from a certain State Board of Health Inspector of Hospitals asking if a cesarean section rate of 20 per cent, which obtained in a certain hospital he had visited, was not a little high! The lowered maternal mortality rate which in good hands now attends the operation will probably incite still further increase in the number of unnecessary operations, —done without heed of the future. Hence, let us emphasize more than we have in the past this crippling—indeed, this quasi-sterilizing—effect of cesarean section.

This article is replete with other instructive data, should help reduce the incidence of unnecessary sections and deserves the study of every physician who practices obstetrics.—Ed.)

## THE HAZARD OF ANOXIA DURING NITROUS OXIDE ANESTHESIA

A. L. BARACH AND E. A. ROVENSTINE

Anesthesiology, 6: 449-61, 1945

The authors show that the current use of anoxia as an adjunct to nitrous oxide anesthesia has been the cause of death from asphyxia, psychoses from

## OPERATIVE OBSTETRICS

### TEN YEARS OF CESAREAN SECTION AT THE BOSTON LYING-IN HOSPITAL

FREDERICK C. IRVING

*Am. J. Obst. & Gynec.*, 50: 660-680, 1945

This report covers 1887 consecutive cesarean sections performed at the Boston Lying-In Hospital during the ten years from 1934 to 1943 inclusive. Since these operations occurred in a total series of 45,216 deliveries, and since the results obtained are compared, in all major complications, with those achieved by other methods, the study covers a vast clinical experience. The incidence of the operation (as calculated from the above figures) was 4.2 per cent, but this frequency was in part due to the relatively large number of cesarean sections performed on private patients. Among 33,688 deliveries on the public ward service there were 1094 abdominal deliveries (3.2 per cent), while among 11,528 deliveries on the private service, the number was 793 (6.7 per cent).

The relative danger of cesarean section is poignantly stressed at the outset by a chart which shows: (1) Normal delivery was 15 times safer for the mother than cesarean section and  $2\frac{1}{2}$  times safer for the infant. (2) Low forceps was  $7\frac{1}{2}$  times safer for the mother than cesarean section and just as safe for the infant as normal delivery. (3) On the other hand, midforceps was almost as dangerous for the mother as cesarean section and about 8 times more dangerous for the infant. (4) Provided it is indicated, therefore, cesarean section compares favorably with midforceps as a method of delivery.

About three-fourths of the operations were elective. As regards type, 54.6 per cent were classical, 36.4 per cent were lower segment, 6.6 per cent were extraperitoneal and 2.4 per cent cesarean-hysterectomies. In the lower segment group the longitudinal (Kroenig) incision was used in about three-fourths. No significant differences in puerperal morbidity or maternal mortality were observed between the classical and low segment groups. Approximately, one-fourth (24.4 per cent) of the patients were sterilized at the time of operation, chiefly on the indication of one or more previous sections. Two pregnancies following the Pomeroy procedure were encountered.

The main indications for abdominal delivery in 1736 viable pregnancies, in order of their frequency, were: previous cesarean section, 361 cases (20.8 per cent); cephalopelvic disproportion, 256 cases (14.7 per cent); contracted pelvis, 239 cases (13.8 per cent); placenta previa, 202 cases (11.6 per cent); uterine inertia, 178 cases (10.3 per cent); and pre-eclampsia, 130 cases (7.5 per cent). Although the indication of a previous section thus loomed large in this series, it should be noted that between 1930 and 1941, 78 women with previous cesarean section were delivered 118 times. More than one-fourth of the operations on private cases were done because of a previous abdominal delivery but only one-eighth of the ward operations. Looking at the incidence of cesarean section

in certain major complications from another viewpoint, 62.5 per cent of all cases of placenta previa were delivered abdominally, the remainder by other methods; 14.2 per cent of the patients with premature separation of the placenta were delivered abdominally, the remainder by other methods; and 2.7 per cent of the cases of pre-eclampsia were delivered abdominally, the remainder by other methods.

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## THE HAZARD OF ANOXIA DURING NITROUS OXIDE ANESTHESIA

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The authors show that the current use of anoxia as an adjunct to nitrous oxide anesthesia has been the cause of death from asphyxia, psychoses from

permanent brain damage, personality defects which may or may not be recognized and impairment in circulatory and respiratory function which may contribute to pulmonary atelectasis, pulmonary edema or cardiac failure. It is proposed in this report to criticize the deliberate use of anoxia as unphysiological, dangerous to life and mental health and without justification in anesthetic practices and to remonstrate against its continued recognition.

In 1911, McKesson introduced the principle of fractional rebreathing into gas anesthesia. His most radical departures from the recommendations of Hewitt, Andrews and others were the induction of anesthesia with undiluted nitrous oxide and the saturation technic. Today the saturation and secondary saturation techniques are not practiced extensively, but the rapid induction with 100 per cent nitrous oxide is popular. Clinically, the available evidence indicates that nitrous oxide should never be administered with an oxygen concentration below 20 per cent. If sufficiently profound anesthesia is not then obtained, other technics should be used rather than resort to asphyxia or even so-called moderate anoxia. Since deaths do occur as a result of nitrous oxide anesthesia, one must assume that technical errors are often committed or the present approved principles for administering nitrous oxide are themselves at fault.

Several instances of lesions produced by anoxia during nitrous oxide administration are set forth. In order to protect the patient-public against death or permanent impairment in mental functioning, asphyxia of very short duration must be regarded as a grave hazard to the great majority of individuals.

Cylinders containing 80 per cent nitrous oxide and 20 per cent oxygen will provide an unvarying concentration of these gases with a cylinder pressure of 700 pounds. The increased cost of such mixtures should not be made the basis of permitting a practice that is dangerous as well as unphysiological, e.g., the use of sub-normal oxygen concentrations in anesthesia.

Finally, the authors believe that the medical profession should be widely informed that so-called "gas oxygen" anesthesia is in many instances a procedure that deliberately exposes the patient to severe anoxia, the results of which may be psychotic invalidism, personality defects, or death from circulatory or respiratory failure.

## THE USE OF LUMBAR ANESTHESIA IN CESAREAN SECTION

J. GRANZOW

Zentralbl. f. Gynäk., 68: 323-30, 1944

In the 13-year period, 1930-1942, lumbar anesthesia was chosen in 442 of the 735 intraperitoneal isthmic cesarean sections performed at the Danzig clinic. The patient was allowed to remain seated for 5 minutes before being placed in the horizontal position on the operating table. In 18.8 per cent of the cases this method was found unpracticable after it had been attempted and other anesthesia

was resorted to. Vomiting and retching were noted in 33 cases. There were 10 maternal deaths in this series but in only one of these could the death possibly be assigned to the anesthesia. The other nine deaths were attributed to diseases complicating the pregnancy. Indications from cesarean section included placenta previa (82 cases), elderly primiparity with primary weakness of labor pains (103 cases) and narrow maternal pelvis (135 cases). Nine of the infants were dead at birth and 12 died before the mother was discharged from the hospital. No injuries to infants that could be attributed to the anesthesia were noted. Asphyxia occurred in 13.35 per cent of the cases as compared with 46.83 per cent among infants born to a series of women given ether anesthesia.

## INTRAVENOUS OBSTETRICAL ANESTHESIA.

### PRELIMINARY REPORT

FREDERICK M. ALLEN

Amer. Jour. Surg., 70: 283-290, 1945

The results of studies on the intravenous use of drugs of the procaine class for relief of pruritis in jaundice cases (Lundy), for painless dressing of burns (Gordon) and for relieving pain after surgical operations (McLachlin) suggested that, although procaine circulating in a low symptomless concentration in the blood does not in normal tissues produce local anesthesia, in regions of injury, pain, inflammation or edema the increased capillary permeability allows the procaine to diffuse into the tissues and anesthetize the nerve endings there. Theoretically, pain not associated with this special vascular permeability would not be relieved. To further test these theories, the author modified extensively the Lundy technique as follows for a variety of clinical trials: (1) The quantity of procaine and strength of solution were greatly increased; (2) the time of infusion was greatly lengthened; (3) saline was replaced by glucose solution in conditions in which edema might be harmful; (4) the range of application was extended to the widest variety of painful conditions.

In the obstetrical trials, of which 12 cases are reported in detail, two grades of dosage were tested. Small dosage, not sufficient to cause dizziness or other subjective symptoms, was found to dull the pains without interfering with the uterine contractions during the second stage of labor but failed to give relief during third-stage delivery and subsequent repair operations. Larger doses (to 10 grams of procaine per liter of solution), given rapidly, induced freedom from pain and a state of dim consciousness in which the patient was more or less unresponsive but retained some awareness and memory of events and was still able to cooperate by bearing down with her abdominal muscles. Delivery and subsequent repairs of any degree could be completed, as long as the procaine infusion was given at the proper rate. Within a few minutes after the infusion

was stopped, the patients were conscious, talked rationally, and had no headaches, nausea or other uncomfortable sequelae. There was no harm to the infants.

The provisional impression was made that the infusion should usually not be begun in the earliest stage of labor, especially in primiparae or patients with mild pains, feeble uterine contractions and the prospect of long labor, as the relief of such pains may be attended by reduction of uterine contractions or a temporary arrest of labor.

The method is now used routinely by the author in the City Hospital. All patients are tested routinely for sensitiveness to the drug but so far no cases of hypersensitivity were encountered. The only difficulties presented were in the form of convulsions which occurred in a few cases. These spasms were brief and subsided within a minute after stopping the infusion and could, apparently, be prevented by preliminary administration of barbiturates.

## OBSTETRICAL ANESTHESIA

SAM S. CLARK

Kentucky M. J., 43: 308-12, 1945

The choice of obstetrical anesthesia has been the basis of severe controversy in both the field of obstetrics and that of anesthesia. The altered physiology and frequent pathology of the parturient serve to complicate the decision. The author presents a short discussion of the advantages and disadvantages of the more frequently used agents and methods. Included in his discussion are chloroform, ether, divinyl ether (vinethene), nitrous oxide, cyclopropane, pentothal anesthesia, spinal anesthesia and continuous caudal. It is the opinion of the author that continuous caudal is the anesthesia of choice for obstetrics and he states that "the future development along this line is awaited expectantly." For inhalation he chooses nitrous oxide analgesia until terminal delivery is possible at which time cyclopropane is supplemented.

The advantages of continuous caudal presented in this report are: (1) complete control of pain from onset of labor; (2) reduction to toxicity to a minimum; (3) infant shows no respiratory depression due to anesthesia; (4) complete relaxation of birth canal speeds first stage of labor; and (5) patient with toxemia of pregnancy tolerates this anesthesia well. Disadvantages presented are: (1) specially trained anesthetist and special equipment necessary; (2) anatomic anomalies may be encountered making administration impossible; (3) danger of infection at injection site due to proximity of rectum; (4) possibility of injecting anesthetic agent into subdural space causing high spinal anesthesia; and (5) this form of anesthesia is practical only in fully staffed and equipped obstetrical hospital with full time coverage in anesthesia.

## SOCIAL AND LEGAL ASPECTS

### PHYSICIANS AND ADOPTIONS

#### EDITORIAL

West. J. Surg., Obst. & Gynec., 53: 296-298, 1945

As important and unpleasant considerations continue to arise in the matter of the relation of physicians to adoption practices in states which are considered to have up-to-date adoption agencies and legislation, this editorial aims to clarify the physician's actual status and prerogatives and the correct *modus operandi* for physicians in such cases. It is restricted only to the problem as it involves the adoption of the offspring of unmarried mothers. The most important point brought out is that the physician has absolutely no place in the current set-up except in a purely professional role. His only prerogative is to give his professional advice relative to the health of the baby for adoption, the foster parents, or both. However, if he has knowledge of a baby for adoption or of a foster family, the proper procedure is to arrange for the placement through the auspices of a licensed child placing agency.

### THE ACCEPTABILITY AND EFFECTIVENESS OF THE CONDOM AS A CONTRACEPTIVE METHOD

CHRISTOPHER TIETZE AND JOHN B. HAGAMAN

Am. J. Med. Sci., 210: 189-195, 1945

This is a report of the first four years of a project conducted in a rural section of Watauga County, N. C. Condoms were offered by a registered nurse, under the supervision of a physician, to 638 married women under 45 years of age. The mean age of the wives was 29.3 years, the mean duration of marriage 10.3 years, and the average number of children ever born per marriage 3.2. Contraceptive techniques had been used by 45 per cent of the couples and were being used at the time of first interview by 38 per cent. At the first visit the nurse explained the use of the condoms and recorded the history of the patient's exposure to pregnancy and of the use and non-use of contraceptive techniques for each month of the patient's married life, as well as of each pregnancy and its termination. Supplies of condoms (Trojans) were given and follow-up visits were made at intervals of about six months. In calculating pregnancy rates per 100 years of exposure, both before and after the first interview, allowance was made

for periods during which pregnancy cannot occur because of pregnancy, abstinence, etc. The following formula was used:

$$\text{Pregnancy rate} = \frac{\text{Total number of conceptions}}{\text{Total months of exposure}} \times 1200$$

During the pre-interview period those who accepted supplies had had a pregnancy rate of 125 per 100 years of exposure for first pregnancies and of 64 for later pregnancies. The post-interview pregnancy rate was 11 per 100 years of exposure, including instances of irregular use. Among those with previous experience at birth control this figure was reduced to 6 second and subsequent pregnancies per 100 years of exposure. Of the couples who were already using the condom at the time of the interview, 91 per cent accepted the supplies; among those using other methods and those not practicing contraception, the proportions of acceptors were, respectively, 49 and 48 per cent. Reasons given for non-acceptance were natural or operative sterility (28 per cent), religious or moral objections (25 per cent) and desire for a baby (13 per cent). The proportions of those who accepted the supplies and were still using condoms after varying lengths of time were 85, 79 and 73 per cent, respectively, after one, two and three years. The complaint of "interference with sensation," the most frequent reason given for discontinuing the use of the condom, was recorded in two-fifths of the classifiable cases. In 38 of 44 instances, discontinuance of the method could be definitely attributed to the husband, and in six to the wife.

## MISCELLANEOUS

### INCIDENCE OF ADVANCED MATERNAL AGE IN MOTHERS OF ONE THOUSAND STATE HOSPITAL PATIENTS

HERBERT BARRY, JR.

*Arch. Neurol. & Psychiat.*, 54: 186-91, 1945

The relation of advanced maternal age to a number of pathologic conditions in the offspring has been previously demonstrated. In general, however, the age of mothers at the time of birth of children who subsequently become psychotic has been almost universally ignored. It is evident that advanced maternal age is related in some manner to mongolism.

The author has studied a series of 1,000 case histories from a state hospital and the results are presented in this report. Of the 1,000 patients, 94 (9.4 per cent) had mothers who were over 40 years of age at the time of the patient's birth. In the same series of patients, 174 (17.4 per cent) had mothers who died before the patients were 20 years old. Paradoxically, there was a high death rate among the younger mothers, with a relatively low mortality rate among the mothers over 40 years of age.

The evidence which is available indicates an excessive number of older mothers for mental hospital patients. The finding that many patients had experienced the death of their mothers during childhood has been previously noted. The relation between psychosis and maternal mortality might be interpreted in several ways: (1) eventual psychosis in the offspring as a consequence of emotional trauma; (2) resulting deterioration of the physical and emotional environment of the children; (3) disrupted family constellations and emotional tensions; (4) the relation might be incidental to some more immediate factor, such as the age of the mother; or (5) death of the mother might be evidence of deficient biologic stamina.

A supposition might be that mongolism as well as erythroblastosis results from biochemical changes in the maternal organism which develop or become accentuated with age.

In view of the well known hazards of statistical argument the author presents these and the major findings as preliminary, pending adequate confirmation.

(The most clear-cut relationship between advanced maternal age and abnormal off-spring is found in mongolism. In 1925 Marston (*Psychol. Clin.*, 16: 135-140, 1925) showed that 37 per cent of the mothers of mongolian idiots were 40 years of age or over at the birth of their defective off-spring, whereas in the population at large the percentage of births to mothers of 40 or over lies somewhere between 2 and 4 per cent. The fact that 9.4 per cent of the 1000 mentally defective inmates of a state hospital described in this article were born to mothers of 40 or over is very suggestive and if it can be confirmed, will be further evidence, and from a new point of view, that mothers should be young for optimum results.—Ed.)

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her with the procedure and her child and prevents the baby from associating feeding time with sleeping.

Many other hours of nursing time have been saved through the cooperation of physicians, hospital administrators, nurses, public health agencies and other organizations. Changes have taken place in procedures long considered essential but which upon careful analysis proved to be alterable.

CATHARINA GEERTRUIDA SCHRADERS AND HER DIARY. A  
NOTE ON THE HISTORY OF OBSTETRICS AND ESPECIALLY  
ON THE HISTORY OF PLACENTA PREVIA

ANDREW A. MARCHETTI

Am. J. Obst. & Gynec., 50: 160-67, 1945

This account of the life and work of Catharina Geertruida Schraders (1655-1746), a Dutch midwife, is based on two articles, one by Dr. Arie Geyl of Dordrecht published in 1897, and the other by Dr. Nuyens of Amsterdam published in 1926. These authors had obtained their data from the Diary in the Library of the University of Amsterdam. Catharina Schraders' obstetric career began in 1693, a year after the death of her physician husband, and ended in 1745, when she was 90 years old. During this time she recorded over 4,000 deliveries, under all kinds of circumstances and in all ranks of society, with 90 fetal deaths (2.25 per cent) and 15 maternal deaths (0.375 per cent). According to Geyl she reported six real cases of placenta previa and one doubtful one. It appears that she recognized the anatomy of placenta previa and its clinical dangers independently of Portal, whose *La Pratique des Accouchemens* appeared in Dutch translation in 1690. The status of midwifery in Holland and other European countries at the time is briefly reviewed.

## NURSING TECHNIQUES IN MATERNITY HOSPITALS

RUTH M. OLSON AND MARTHA L. CLIFFORD

Am. J. Pub. Health, 35: 1199-1202, 1945

The tremendous increase in births in recent years combined with the decrease in hospital personnel has presented a major problem in furnishing adequate hospital care. The authors discuss in this report the nursing aspects of the problem. They present streamlined nursing techniques which have been carried out successfully in Connecticut with the resultant saving of nursing hours and continued adequate care for a greatly increased number of mothers and babies.

The four major areas of nursing service in a maternity hospital are: (1) labor and delivery service; (2) care of postpartum mothers; (3) care of newborn infants; and (4) preparation of formulae.

Since constant supervision of patients during labor and delivery is essential, these services should be fully staffed both day and night.

Postpartum care of the mother can be greatly simplified without jeopardizing the mother's safety. A simple method of perineal care carefully carried out once a day and following defecation with application of sterile pads has proved safer than more frequent care which tends to become careless due to pressure of work. Bedpans may be kept at the bedside and be sterilized after discharge. Newspaper bedpan-covers may be discarded after one use and will prevent contamination by cloth covers used several times. The procedure of swabbing the breasts before and after each nursing with boric acid has proved itself an ineffectual ritual. Careful bathing of the breasts once daily followed by covering them with a clean towel has proved quite satisfactory. Discontinuing the use of breast and abdominal binders except for specific reason is another means of saving nursing time.

The two principles involved in nursing care for newborn infants are: (1) prevention of introduction of infection from outside; and (2) prevention of infection between infants. The number of persons entering the nursery should be strictly limited to the number necessary to give care. Any person entering should wear a gown and mask and doctors and nurses should wash their hands thoroughly before and after handling each baby. The care of babies should be completely individualized and everything contacting the baby should be clean and, if possible, sterilized. A modified Sanford method is recommended in which the baby is wiped at birth and is not oiled or washed until discharged. Reduction of the frequency of weighing will save nursing time.

Formulae should be prepared and kept under strict aseptic conditions by the nursery nurse or by a dietician. If a nursery nurse, who is familiar with each baby, prepares the formulae she can choose and place on each baby's bottle the right type of nipple and so save time and prevent contamination of changing nipples. It is wise to have the mother feed the baby its bottle since this acquaints

her with the procedure and her child and prevents the baby from associating feeding time with sleeping.

Many other hours of nursing time have been saved through the cooperation of physicians, hospital administrators, nurses, public health agencies and other organizations. Changes have taken place in procedures long considered essential but which upon careful analysis proved to be alterable.

CATHARINA GEERTRUIDA SCHRADERS AND HER DIARY. A  
NOTE ON THE HISTORY OF OBSTETRICS AND ESPECIALLY  
ON THE HISTORY OF PLACENTA PREVIA

ANDREW A. MARCHETTI

Am. J. Obst. & Gynec., 50: 160-67, 1945

This account of the life and work of Catharina Geertruida Schraders (1655-1746), a Dutch midwife, is based on two articles, one by Dr. Arie Geyl of Dordrecht published in 1897, and the other by Dr. Nuyens of Amsterdam published in 1926. These authors had obtained their data from the Diary in the Library of the University of Amsterdam. Catharina Schraders' obstetric career began in 1693, a year after the death of her physician husband, and ended in 1745, when she was 90 years old. During this time she recorded over 4,000 deliveries, under all kinds of circumstances and in all ranks of society, with 90 fetal deaths (2.25 per cent) and 15 maternal deaths (0.375 per cent). According to Geyl she reported six real cases of placenta previa and one doubtful one. It appears that she recognized the anatomy of placenta previa and its clinical dangers independently of Portal, whose *La Pratique des Accouchemens* appeared in Dutch translation in 1690. The status of midwifery in Holland and other European countries at the time is briefly reviewed.

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# Maternal Mortality Reports

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*(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.)*

*Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)*

## CASE NO. 6

The patient was a 36 year old white multipara who was admitted to the hospital on December 9 after having been labor in another hospital for 4 days without progress. Her family and personal history was noncontributory. Both of her previous pregnancies were uneventful and terminated in normal spontaneous deliveries followed by normal postpartum periods, the last occurring 10 years ago with a full term living child weighing 8½ pounds.

She was seen for the first time during this pregnancy at about the sixth month at which time her blood pressure was 170 mm. systolic and 110 mm. diastolic. She was put on a diet low in protein content and salt. From this time until her admission to the first hospital the blood pressure varied from 150 mm. to 200 mm. systolic and from 90 mm. to 110 mm. diastolic. The urine showed a trace of albumin on several occasions. The estimated date of confinement was November 18, but she was not admitted to the first hospital until December 4, at which time her membranes were found to be prematurely ruptured. Because of the failure of labor pains to begin, she was sent home on the following day. On December 6 labor pains began and the patient was readmitted to the hospital. Progress was apparently satisfactory and at 9 P.M. the cervix was thought to be fully dilated. She was prepared for delivery and on vaginal examination the full dilatation of the cervix was verified, but since the presenting vertex was only 1 cm. below the level of the spines, no attempt was made to deliver the patient at this time.

A consultant was called on the telephone and he advised the administration of ½ of a grain of pantopon. At this time the temperature was found to be 100°F., the pulse rate 120 per minute and the blood pressure 180 mm. systolic over 110 mm. diastolic. The urine showed a 1+ albumin.

Efforts to stimulate pains, consisting of castor oil and several injections of pitocin, failed to produce sufficient uterine contractions to effect delivery of the fetus and the patient was allowed to remain undelivered throughout December 7 and December 8. At this time x-ray examination of the abdomen revealed a fetus lying in a longitudinal position with the back to the right and anterior and with a markedly flexed head. On this day a catheterized specimen of urine showed a moderate amount of gross blood and a 2+ albumin. The blood pressure was 170 mm. systolic and 100 mm. diastolic.

The same consultant was again telephoned and he advised further efforts to stimulate pains along the lines previously attempted. This was ineffectual and it was decided to call a second consultant who advised the immediate transfer of the patient to a second hospital. This was done and the patient was admitted to the hospital at 2:30 P.M. on December 9. She appeared quite toxic and moderately jaundiced. The temperature was 99.8°F., the pulse rate 128 per minute and the respirations 38 per minute. The blood pressure was 165 mm. systolic over 105 mm. diastolic. The abdomen was moderately tense and palpation was difficult especially in both lower quadrants. The height of the fundus was 31 cms. and

the fetus lay in a right-occipito-anterior position. The audibility of the fetal heart sounds was the subject of controversy. She was given some pantopon, and 1000 cubic centimeters each of 5 per cent glucose and normal salt solution. X-ray examination verified the marked flexion of the head mentioned above. The injection of 500 cubic centimeters of whole blood was started and the patient was prepared for vaginal examination and delivery if possible. The cervix was found to be fully dilated as reported, and in addition a large, cystic hydrocephalic head was diagnosed, its lower-most portion lying about 2 cm. above the level of the spines. Hair came off on the examiner's glove and the existence of fetal death was established.

The hydrocephalic head was pierced with scissors and delivery was effected with considerable difficulty. Palpation of the uterine cavity immediately following the delivery of the fetus revealed a large tear in the anterior uterine wall. Laparotomy was performed at once. The placenta was free in the abdominal cavity, and the rupture of the uterus involved the anterior wall of the uterus halfway to the fundus and almost the entire length of the cervix. Two hundred cubic centimeters of free blood were found in the peritoneal cavity. A supravaginal hysterectomy was rapidly performed. The patient received 2500 cubic centimeters of whole blood and 500 cubic centimeters of plasma throughout the time of her delivery and the removal of the uterus. Her condition was poor but she rallied considerably in the next 24 hours. Penicillin therapy was begun at once. Her temperature reached a peak of 101.8°F. on the second day postoperative. Nasal oxygen was given constantly. The urinary output was 2100 cubic centimeters for the first 24 hours and on the next day it was 1100 cubic centimeters. On the third day she voided in bed. At 4 A.M. on December 13 the patient passed a considerable quantity of muddy looking fluid from the vagina following which the temperature rose to 101.4°F., the radial pulse became imperceptible and at 5:10 A.M. respirations ceased.

It was later learned that approximately one hour following the first pelvic examination in the first hospital on December 6, the patient passed several hundred cubic centimeters of blood after which all uterine contractions ceased.

*Discussion:* This case history is almost unbelievable, so many and culpable were the errors. 1. This hypertensive, post-term woman with prematurely ruptured membranes should not have been sent home from the hospital on December 5. 2. If the consultant, who prescribed for the patient over the telephone, had actually seen and examined her, he would (it is hoped!) have spotted the hydrocephalic head; the second consultant did so immediately. This was the crucial error. Had the diagnosis been made at 9 P.M. on December 6, and suitable treatment instituted, the woman would doubtless have survived. 3. Pitocin, of course, killed the patient by causing the uterine rupture. 4. This woman presented two classical signs of uterine rupture, namely, cessation of pain at complete dilatation and grossly bloody urine; and she presented them for two full days and still the diagnosis was not made. 5. Even on x-ray examination the disproportion caused by the hydrocephalic head was missed. 6. With all this story, the consultant when telephoned again still did not see the patient but ordered more pitocin! Here, printable words fail your Committee.

In the second hospital the patient seemed to have received prompt and intelligent treatment, but the colossal errors enumerated above had already wrought fatal damage.

#### CASE NO. 7

The patient was a 23 year old primigravida who registered for prenatal care on September 30. She had been married for 15 months, her last menstrual period having occurred June 5

and the estimated date of confinement March 12. She was of large stature, 5'7" tall and weighed 170 pounds. The external pelvic measurements were ample and the promontory of the sacrum could not be reached on vaginal examination. The blood pressure was 120 mm. systolic, 80 mm. diastolic, and the urine was negative for sugar and albumin on the first visit on September 30.

The patient returned at regular intervals as instructed for her prenatal visits, and on December 6 the blood pressure rose to 150 mm. systolic over 90 diastolic. The urine at this time was negative for albumin. She was put on a low salt diet, rest and sedation. On this regime her blood pressure remained around 140 mm. systolic over 90 mm. diastolic until the patient reached term. The urine was negative throughout pregnancy but there was on repeated occasions a mild amount of edema of the lower extremities. The weight gain was excessive, the patient having gained a total of 45 pounds from the time of her first visit until she entered the hospital on March 14.

She was not in active labor at this time but her membranes had ruptured 8 hours previously. There were some vague irregular contractions of short duration which occurred at infrequent intervals. The fetus presented by the vertex, the presenting part being at a level of about 3 centimeters above the spines. The cervix was long, uneffaced and 2 centimeters dilated. The blood pressure was 146 mm. systolic over 96 mm. diastolic and the urine was negative for albumin.

The patient was given a medical induction consisting of castor oil, enema and pitocin, but the uterine contractions were not increased in severity or effectiveness. In an effort to overcome what appeared to be a primary uterine inertia, the patient was given stilbestrol 50 mg. for two doses and infundin minims 2 every 15 minutes for seven doses, but in spite of this medication the contractions remained of poor quality.

She was allowed to continue in this ineffectual type of labor throughout the day of March 15 with little or no progress. The contractions remained poor, the head high in the birth canal, and the cervix failed to become more dilated. One thousand cubic centimeters of 5 per cent glucose were given on two occasions. After 36 hours of ruptured membranes, the temperature rose to 101°F. and the pulse rate to 94 per minute.

At this time it was decided to deliver the patient by the abdominal route and under nitrous oxide, oxygen and ether anesthesia a classical cesarean section was performed. A living child weighing 7 pounds 13 ounces was delivered. The patient was given sulfa therapy starting immediately postoperatively but in spite of this the temperature and pulse rate remained elevated. On the fifth day after operation the abdominal incision was examined and a considerable amount of pus was found on slight probing. The entire incision soon separated down to the fascia. On the seventh day after operation, she became distended and it soon became obvious that there was a peritonitis present. The distension and vomiting became worse and in spite of repeated transfusions, sulfa drugs, oxygen and other measures, the patient died on the eleventh postoperative day. Exploration of the wound revealed considerable free pus in the peritoneal cavity, an unhealed uterine incision, and partial intestinal obstruction.

*Discussion:* Whatever else might be said in criticism of the handling of this case, certainly the performance of a classical cesarean section on an obviously infected patient did not add to the safety of the individual. The performance of a low cervical section would have been a better procedure and the removal of the uterus after the section probably the most advisable thing to do. The publication of Porro's monograph in 1876 was followed by the saving of many lives.

The performance of an extraperitoneal section should have been seriously considered in this case. This type of operation is of great advantage in indicated cases and it is deplorable that more obstetricians throughout the country are not skilled in its technique. This was considered a preventable death.

## CASE NO. 8

The patient was a 29 year old colored multigravida who was admitted to the hospital on May 17 with the history of having been delivered at home of a full term living child 12 days previously. Her previous pregnancies and deliveries were normal. The prenatal course and the first and second stages of this labor are reported as having been uncomplicated. Following this, however, the attending physician was unable to deliver the placenta. Massage of the uterus and repeated attempts using the Credé method of expression failed to complete the third stage of labor. These efforts continued for about 12 hours during which time the patient lost a considerable amount of blood by vagina. Finally the placenta was manually removed by the attending physician at home without too much effort to maintain an aseptic technique.

For several days the patient's condition was considered satisfactory but then she developed a severe chill followed by an elevation of temperature. Her physician ordered some sulfa therapy which the patient took very irregularly. Following the initial chill and rise in temperature the patient had several chills subsequently, suffered with severe headaches and noticed some shortness of breath. She developed some tenderness in the lower abdomen which seemed somewhat improved just prior to admission to the hospital on her twelfth day postpartum.

On admission the patient had a temperature of 106°F., a pulse rate of 145 per minute, and the respirations were 48 per minute. She appeared acutely ill and her respirations were quite shallow. Mentally she appeared slightly cloudy. There was marked tenderness of the lower abdomen and the patient showed evidence of anemia. Examination of her blood showed 1.17 million red blood cells, 19,650 white blood cells, 3 grams of hemoglobin (20%) and a color index of .85. A blood culture taken on the day of admission showed no growth on prolonged incubation.

Despite sulfa therapy, transfusions at frequent intervals and other treatment, the patient continued to run a spiking type of temperature chart with daily rises to 106°F. and declines to 101°F. and 102°F. On the second day after admission she began to complain of abdominal pains, developed some vomiting and began to show marked abdominal distension. This continued throughout the rest of the hospital course with periodic alleviation with treatment but the relief was always temporary. Treatment included enemata, Wangenstein drainage, and the insertion of the Miller-Abbott tube. In spite of repeated transfusions and the administration of iron and liver extract the patient's red blood cell count and hemoglobin responded poorly.

On the seventh hospital day a well localized abscess mass could be palpated in the left lower quadrant. The patient continued to run a spiking fever averaging 104°F. at its peak. On the twelfth hospital day which was the twenty-third day postpartum, her temperature dropped slightly and for the next week averaged about 102°F. at its upper level. However, in spite of all efforts to combat the infection, the patient's course was gradually downhill and she died on her thirty-second day following delivery.

*Discussion.* This patient should have been sent to a hospital for further management when the ordinary external attempts to promote placental separation and expulsion proved definitely of no avail. She was delivered in a large city where excellent hospital facilities and obstetrical consultation were readily available. Manual removal of the placenta, even in the best maternity hospital, is never to be undertaken lightly. It calls for meticulous aseptic technique and should never be performed in the home unless fulminating third stage hemorrhage demands it as an emergency procedure. This physician's repeated attempts at Credé expression over a 12-hour period despite continued bleeding, and his failure to make use of readily available hospital facilities and consultation were plainly responsible for this death. The transfer of the patient to a hospital

after two hours, let us say, of placental retention, skillful manual removal under aseptic conditions and immediate blood transfusion if necessary would doubtless have saved the patient's life.

#### CASE NO. -9

The patient was a 19 year old white primigravida who was admitted to the hospital on September 25 at 10:45 A.M. in early labor. Her family and personal history was noncontributory. Her last menstrual period was on December 13 and the estimated date of confinement September 20. The entire prenatal course was essentially normal. The external pelvic measurements were within normal limits, but no internal pelvimetry was done.

On admission to the hospital the patient was having pains every 20 to 30 minutes. The blood pressure was 125 mm. systolic, 80 mm. diastolic. Labor pains continued which were weak, irregular, and not very frequent. At 5:20 A.M. the next morning an attempt was made to stimulate uterine contractions by administering quinine, castor oil and 2 doses of pitocin of 3 minims each. Following this medication the labor pains became much stronger and occurred at 3 minute intervals. At 12 noon the membranes ruptured spontaneously. On rectal examination at this time the cervix was thought to be fully dilated and both feet were found to be presenting. The patient was immediately taken to the delivery room and at 12:40 P.M. she was anesthetized, an episiotomy performed and the fetus extracted up to the head which was finally delivered with forceps after prolonged efforts to extract it manually. The baby was stillborn and weighed 9 pounds. The placenta was expressed without difficulty but there was a considerable amount of free bleeding immediately postpartum which was controlled by intravenous pitocin and ergotrate. The cervix was found to be intact according to the report. The patient's pulse rate was 160 per minute and it was thought advisable to give her 500 cubic centimeters of 10 per cent glucose intravenously. The patient was returned to her room in fairly good condition at 1:45 P.M.

At 2:00 P.M. she began to bleed very freely and the uterus on abdominal palpation was found to be quite relaxed. Her private physician was consulted over the telephone and upon his advice the hospital interne packed the patient's *vagina* in bed at 2:30 P.M. In a very short time she bled through the vaginal pack and at 3 P.M. the *vagina* was repacked with a fresh gauze pack. This was done by her own physician who performed the procedure with the patient still in her own bed and following which he immediately left the hospital. The patient continued to bleed, however, and the physician was again called and he instructed the interne over the telephone to repack the *vagina* with a larger pack. This was done at once with the patient still in her bed. By this time the patient was in shock and another 500 cubic centimeters of 10 per cent glucose were given intravenously. The patient was now matched and grouped in an effort to secure blood for a transfusion. At 4:45 P.M. adrenalin, coramine and alpha lobelin were given to the patient. At 5:30 P.M., 500 cubic centimeters of whole blood were being given and at 5:55 P.M. the patient died. Permission for autopsy was denied.

*Discussion:* This case was so badly handled that it is difficult to know just where to begin. The failure to determine the size of the pelvis was probably due to reliance on external pelvimetry as an accurate index of the type of pelvis involved. Certainly an attempt to measure the diagonal conjugate and the pelvic outlet, combined with roentgenpelvimetry and roentgencephalometry if they were available, would have given much valuable information. If nothing else, the attendant would have known that he was dealing with a large baby presenting by the breech in a primigravida. The use of quinine for the induction of labor has been abandoned by most obstetricians in view of reported deleterious effects on the infant.

In addition, the return of a patient to her room less than an hour postpartum who had bled so freely was bad practice. The failure to give some whole blood at this time in addition to the glucose was neglect also. But everything pales into insignificance when it is compared to the inexcusable advice to the interne to pack the vagina to control bleeding due to a relaxed uterus. Obviously, this case should have been handled in the delivery room where uterine packing or bimanual compression of the uterus, or both, should have been carried out, and in addition, whole blood transfusion started before 3 P.M. The repeated vaginal packings with the patient in bed and the failure to give blood until the patient was about to expire were such reprehensible errors as to leave no doubt concerning the preventability of this death.

## CASE NO. 10

The patient was a 33 year old white multigravida whose family and personal history was noncontributory. The first pregnancy had been complicated by a toxemia associated with convulsions. This labor was terminated instrumentally per vaginam with a full term stillborn infant. Full term living infants were delivered spontaneously in the second, third and fourth pregnancies. There was no evidence of any toxemia in these remaining three pregnancies. All four infants were delivered vaginally, the last three being still alive and well.

The history of the present pregnancy reveals that the last menstrual period was on August 2. The patient first reported to her physician on February 25. Her estimated date of confinement was May 9. On her first visit the blood pressure was within normal limits, the urine was negative for albumin, and her general physical examination was negative except for a large umbilical hernia.

The pregnancy progressed normally except for a very mild hypertension which developed late in April. *At the patient's request the attending obstetrician agreed to deliver her by cesarean section and repair the umbilical hernia at the time of the abdominal operation.*

She was admitted to the hospital on May 7 for operation the following morning. On admission her general physical examination revealed her heart and lungs to be normal, the blood pressure 128 mm. systolic over 80 mm. diastolic, and the hemoglobin 60 per cent. An elective classical cesarean section was done at 8:25 A.M. on May 8 under ether anesthesia. A full term live born infant was delivered but the patient had such profuse bleeding from the uterine incision that it became necessary to perform a hysterectomy before the hemorrhage could be controlled. Following this the umbilical hernia was repaired. The total operation required two hours, and at its conclusion the patient was given 500 cubic centimeters of whole blood.

She was returned to her room in fairly good condition after having recovered from the anesthetic. Twenty-four hours after the operation there was a slight amount of distension. Enemata were very effectual but in spite of pitressin and other medication the distension persisted and by the next morning there was some vomiting. Intravenous glucose was begun and the patient was given turpentine stupes. Several enemata were given throughout the day without effect. Nasal drainage was begun 60 hours postoperatively to relieve upper abdominal distension, and as flatus was being passed and intestinal movements were audible, castor oil was given on the morning of the 11th, 72 hours after the operation. At 4 P.M. the patient had a small bowel movement. In spite of this at 10 P.M. her condition was definitely worse and she was given 500 cubic centimeters of 2 per cent salt solution followed by a 500 cubic centimeter blood transfusion. Following this there was definite improvement in her condition and some flatus was passed along with a small fluid stool.

The abdominal distension continued, however, and at 4 A.M. on May 12 the patient was given 80 mg. of novocaine intraspinaly. Immediately before this treatment her blood

pressure was 138 mm. systolic, 90 mm. diastolic. Shortly after the intraspinal injection the blood pressure had dropped to 105 mm. over 50 mm. About one-half hour later the patient expelled a large fluid stool and shortly thereafter said she felt fine.

An hour and a half later the patient became maniacal, left her bed and required restraint. Her condition rapidly became grave and in spite of supportive therapy she died about 5 hours later. The temperature was never above 100°F. until the patient became acutely ill on the evening of the third day after operation when it rose to 100.6°F., and reached 103.6°F. rectally just before death.

Partial autopsy showed that there was no peritonitis, but there was a thrombosis of the left hypogastric vein along with a paralytic ileus. There was no evidence of a pulmonary embolus. Brain autopsy was not obtained.

*Discussion:* This patient would doubtless be alive had she been allowed to deliver spontaneously instead of being subjected to an abdominal operation for which there was no good indication. The use of the low cervical section or laparotrachelotomy in preference to the classical Säger operation has many advantages. Regardless of the type of operation to be performed, it is only reasonable to demand a good indication for so serious a procedure. The use of the cesarean section as an easy way out of a perplexing situation, or worse still at the request of the patient, is most inexcusable.

#### CASE NO. 11

The patient was a 26 year old white primigravida who was admitted to the hospital on April 18 complaining of abdominal pain. The family and personal history was noncontributory. Her last menstrual period was on August 3 and the estimated date of confinement on May 10. The prenatal course was essentially normal until April 18 when she complained of rather severe abdominal pain.

On admission to the hospital the temperature was 99.8°F., the pulse rate 100 per minute, and the patient within a few weeks of term. The abdomen seemed rather more distended than was normal for a pregnancy of this duration. The blood pressure was 116 mm. systolic, 70 mm. diastolic, the hemoglobin 86 per cent, the urine showed a trace of albumin, the fetal heart was heard in the left lower quadrant, and there was no external bleeding.

In an effort to determine the exact cause of the abdominal pain, several possibilities presented themselves as the most likely in view of the fact that the patient definitely was not in labor. A premature separation of a normally implanted placenta was considered, only to be ruled out on further examination; the patient's symptoms were too severe to be due to a simple hydramnios, and some acute intra-abdominal condition appeared to be a likely cause for her illness.

It was decided to keep the patient under observation a little while, and during the next few hours she began to have some uterine contractions. Labor continued and after a prolonged labor of almost 36 hours, delivery of a 7 pound living infant occurred on April 19 at 9:15 P.M. There was no abnormal bleeding following this spontaneous delivery but there was considerable distension which persisted in spite of treatment. The temperature remained elevated but did not go beyond 101.5°. Intravenous glucose, physostigmine and Wangenstein drainage failed to relieve the distension and surgical consultation was sought. The consultant found evidence of fluid in both flanks and stated that it was his impression that the patient was suffering from "gastric atony, pyloric spasm and possibly some intra-abdominal condition." He recommended supportive therapy and attempts to reduce the distension by gastric drainage. On April 30 a gynecological consultation was obtained and a diagnosis of intestinal obstruction was made at that time. Under palliative treatment the patient showed no improvement. The temperature and pulse rate continued to be elevated and the distension was still marked in spite of sulfa therapy, blood transfusions,

gastric and duodenal drainage. About this time the perineum broke down resulting in a rectovaginal fistula. On May 11 an x-ray examination gave evidence of a mass in the right side of the abdomen displacing the intestines. Following this, pelvis examination suggested an intra-abdominal abscess formation. The patient complained of several chills about this time. On May 27 an exploratory laparotomy was performed and through a midline incision a mass was entered which contained pus, fecal material and undigested food particles. This opening was packed with iodoform gauze and the abdominal incision drained. The patient had a number of chills following this operation and her condition did not seem to improve much. The temperature chart became spiking in character and she complained of severe abdominal pain. Many blood transfusions, much intravenous glucose, and multiple vitamins in large quantity were given. Her condition grew steadily worse in spite of occasional temporary respites, and on June 13 she rather suddenly developed cardiac dilatation and vasomotor collapse and died, almost 2 months after admission to the hospital with a complaint of abdominal pain.

*Discussion:* This fatality was the result of failure to diagnose acute appendicitis and for this reason was classified as preventable. Diagnosis of this complication is not easy for many reasons. The appendix is displaced upward after about the third or fourth month of pregnancy, and this combined with other factors makes difficult the differential diagnosis between appendicitis and pyelitis, ureteral stone, abruptio placentae during late pregnancy, a twisted cyst and many other conditions. Perforation and suppurative peritonitis are most serious during pregnancy. Abortion and premature labor are quite common and the maternal mortality is very high, especially at or near term.

The possibility of appendicitis should always be kept in mind by the obstetrician even though it is not a very common occurrence. Early diagnosis is most important and early operation results in a relatively low death rate. Recurrent attacks of appendicitis should be treated by appendectomy before pregnancy occurs. A patient with a history of appendicitis should not be operated upon during pregnancy unless a recurrence takes place; and a normal or chronic appendix should not be removed at the time of cesarean section (performed for some other indication) because infection may be transferred from the appendix to the uterus.

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those which can be seen in ordinary sections with the microscope have been cited also in our foregoing description of the rhesus corpus luteum of the 10th to the 12th day, i.e., collapse of the capillary blood vessels, increase of visible lipids in the granulosa luteum cells, and diminution of size of some of these cells. We have, however, not interpreted these as necessarily signs of degeneration.

If the animal becomes pregnant, no further changes occur in the corpus luteum between days 12 and 19 after ovulation, approximately. From about day 19 to day 24 the corpus luteum is in transition to the pregnancy type. After day 24 it is in the typical pregnancy stage. The corpus luteum of the nonpregnant animal cannot be distinguished from the corpus luteum of pregnancy of the same age, until visible degeneration of the former sets in, about day 13 after ovulation. The theca interna cells retain their identity after ovulation. They are not distinguishable during the period of days 4 to 6, but afterward can sometimes be distinguished. In the corpus luteum of pregnancy and the corpus aberrans the theca interna cells or paralutein cells are readily distinguishable in the bases of the folds and at the periphery of the corpus. The blood vessels of the corpus luteum are derived from the capillary net of the theca interna. The fibroblast-like cells which produce the connective tissue of the cavity apparently come from the invading blood-vascular endothelium. There is usually no hemorrhage in the corpus luteum at the time of menstruation. The corpus luteum of pregnancy, though sometimes moderately cystic, shows no systematic tendency in this respect.

(The author, whose pioneer work in establishing the physiological rôle of progesterone is well known, has long been one of our country's outstanding investigators in the field of reproductive physiology. He is now the Director of the Carnegie Institute of Embryology, and like his two great predecessors in that office, Mall and Streeter, his guidance has yielded a valuable yearly output of scientific contributions from that institution. Many of these bear very importantly on our clinical problems in gynecology and obstetrics. Corner's studies are based on corpora lutea in the rhesus monkey, and gynecologists will be interested to find that they corroborate similar studies in the human. Corner, however, makes no mention of the four stages (proliferation or hyperemia, vascularization, maturity and retrogression) into which the life cycle of the human corpus luteum was divided, as far back as 1911, by Meyer, who first described this cycle. Nor does he comment on the "proliferation" phase, concerning the existence of which there was some controversy in 1932 between Meyer and the French investigator, Moulounguet. As a matter of fact, Corner specifically mentions that no mitoses were found in the 2 one day corpora of his series, although Meyer reported these in the earliest phase of the corpora lutea. Finally, Corner appears to be hesitant about accepting Brewer's recent conclusion that the corpus luteum begins to retrogress at about the 22nd day of the cycle, much earlier than was formerly generally believed.—Ed.)

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# Gynecology

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## ENDOCRINOLOGY

### DEVELOPMENT, ORGANIZATION, AND BREAKDOWN OF THE CORPUS LUTEUM IN THE RHESUS MONKEY

GEORGE W. CORNER

Contributions to Embryology, No. 204, Carnegie Institution of Washington  
Publication 557, 117-146, 1945

The report is based on 107 corpora lutea of the rhesus monkey (*Macaca mulatta*, *Macacus* or *Pithecus rhesus*) and deals with appearances revealed by routine histological methods. The menstrual cycle of this animal has a typical length of 28 days. Ovulation most frequently occurs on or about the 13th day after beginning of the last menstrual flow. Variations in the cycle are, however, frequent and large. Before rupture of the mature follicle the granulosa cells become loosened and are drawn into spindle shape, with a tendency to radial alignment. The nuclei stain very densely. After ovulation there is a progressive series of changes, as indicated in the tabular summary (p. 144). Blood vessels begin to invade the granulosa about day 2. The granulosa cells present definite epithelioid characteristics about day 4. The blood vessels reach the inner part of the lutein wall about day 4. At this time capillary sprouts and fibroblast-like cells (apparently derived from the endothelium) enter the cavity. By day 6 the blood-vascular pattern of the corpus luteum is being completed by the development of venous channels in the inner part of the lutein wall. Organization of the corpus luteum may be considered complete by days 7 to 9. Definite connective tissue now begins to appear in the cavity.

If the ovulation did not result in pregnancy, the first definite signs of degeneration are seen about day 13 after ovulation, that is to say, day 26 of the cycle dating from the last menstruation. These dates relate, of course, to the modal 28-day cycle only. Before the onset of menstruation, degeneration is evidenced by extensive lipid vacuolation. About the time when external menstruation begins (day 28 of the modal cycle), nuclear pyknosis and fragmentation are seen, some of the cells are cytolized, and others shrink by contraction of cytoplasmic volume.

Brewer (Brewer, J. L., *Am. J. Obst. & Gynec.*, 44: 1048-1059, 1942) has cited evidence which has led him to believe that the human corpus luteum is degenerating after the 8th or 10th day dating from ovulation. Of these evidential facts,

(It is curious and difficult to explain, that stilbestrol should have been so effective in a case of pseudohermaphroditism of this type, and it is possible that the early age at which this treatment was begun might have been a factor. In an adult case of this type which I observed some years ago, estrogens had been given in large doses from time to time for a good many years, without any noticeable benefit. This patient later came to autopsy, following exploration and resection of the adrenals, which showed remarkable cortical hyperplasia, with no neoplasm in either the adrenals or any of the other endocrine glands. In this variety of female pseudohermaphroditism the external genitalia are rather characteristic of the type described in the case of McIntosh and Brown. It is in this group too, that a rudimentary vaginal canal is often actually present, but it opens into the posterior wall of the urethra some distance, perhaps only a centimeter or so, above the external orifice.—Ed.)

## INFLUENCE OF RELAXIN ON MAMMARY DEVELOPMENT IN SEXUALLY IMMATURE FEMALE RATS

M. HAMOLSKY AND RHODA C. SPARROW

Proc. Soc. Exper. Biol. & Med., 60: 8-9, 1945

The only physiological action so far established for relaxin is relaxation of the pelvic ligaments in the guinea pig. This paper demonstrates the effect of relaxin on the mammary glands of immature female rats.

All animals used for the experiments were immature female rats which had been ovariectomized at 30 days after birth. After 6 days of postoperative rest they were injected daily with estradiol for 13 days. They were then divided into groups and subjected to these experiments. One group was given estradiol, progesterone and relaxin, a second group was given estradiol and progesterone, a third group was given estradiol and relaxin and a fourth group was given progesterone and relaxin.

These experiments showed that estradiol, progesterone and relaxin given together will cause mammary gland growth and lobulation in immature ovariectomized female rats. The authors were unable to obtain mammary gland growth and lobulation with any 2 of these hormones. When the animals were hypophysectomized following pretreatment and then injected with estradiol, progesterone and relaxin, the mammary glands remained immature.

The authors believe therefore that an interaction of relaxin, estradiol and progesterone stimulated mammary gland growth and lobulation in these animals. Hypophysectomy either removed one or more of the hormones necessary for the interaction to take place or so changed bodily conditions (hormonal or otherwise) that growth of the glands was not obtained. 4 figures.

ADRENOGENITAL PSEUDOHERMAPHRODITISM TREATED  
WITH STILBESTROL

C. BERKELEY MCINTOSH AND WILLIS E. BROWN

*J. Pediat.*, 27: 323-327, 1945

Attempts to demasculinize a patient with adrenogenital pseudohermaphroditism by the administration of stilbestrol; and the results of this trial, are discussed. The patient was first observed at the age of five years. Although the genitalia were not characteristic of either sex the child had been reared as a girl. She had grown at an abnormally rapid rate and at the age of five years was 49.3 inches tall and weighed 62.7 pounds. An older sibling, whose sex had also been in doubt and whose growth had also been rapid, had died of pneumonia at the age of six years. The autopsy of this sibling was reported to have revealed marked hypertrophy of the clitoris, an infantile uterus, normal ovaries, a fully developed vagina and definite diffuse hyperplasia of both adrenal glands.

Physical examination of the present patient was essentially normal except for her size, a tendency toward a masculine physique and the appearance of the genitalia. There was a large amount of pubic hair, female in pattern. The phallus measured 2.5 inches in length and had a definite glans and prepuce but no urethral opening. No testicles could be palpated. The urethral opening was in a completely hypospadiac position just below the phallus. Well developed labia were present. The vaginal orifice was small and partially obliterated by a membrane. An exploratory laparotomy revealed the presence of normal tubes and ovaries, a rudimentary uterus, and generalized enlargement of both adrenal glands. Determinations for crystalline androsterone from 24-hour urine samples were consistently high (about 22 mg. equivalents). In an effort to reduce the masculinizing effect of the adrenal glands roentgen therapy was employed for two months, without effecting appreciable change in the patient's appearance or in the size of the clitoris. Oral stilbestrol, 5 mg. daily, was then started. At the end of four months the breasts had become developed and axillary hair had appeared. Because of toxic symptoms the dosage of stilbestrol was reduced to 3 mg. daily for four months but no new changes were seen. The dosage was then reduced to 2 mg. daily and continued for another sixteen months. During this time the rate of growth approached normal and the clitoris decreased in size to 1.25 inches. With the exception of the enlarged clitoris and hirsutism of the legs the patient had the appearance of an adolescent girl. As x-rays showed that the epiphyses were nearly closed and it was felt that the stilbestrol might be contributing to the precocious bone maturity, estrogen therapy was discontinued at this time. Plastic operations consisting of amputation of the clitoris and an extension of the vaginal orifice were performed. It is expected that the patient will be capable of performing coitus, but it is doubtful whether the uterus will ever be mature enough to support menstruation or pregnancy.

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EFFECTS OF THYROID FEEDING ON OVARIAN DEVELOPMENT  
IN THE RAT

BENJAMIN H. ERSHOFF

Endocrinol., 37: 218-220, 1945

In the experiments reported, female rats were raised to maturity on diets containing 0, 0.5 and 1.0 per cent dessicated thyroid, respectively. All groups received sufficient quantities of yeast (12.0 per cent) to maintain growth. The other constituents of the rations were sucrose, 61.5 per cent; Vitamin Test Casein, 22.0 per cent; and Sure's Salt Mixture No. 1, 4.5 per cent. A marked inhibition of ovarian development was observed both grossly and histologically in the thyroid-fed rats; ovarian weights averaged 20.0 and 21.3 milligrams, respectively, for the animals in the 0.5 and 1.0 per cent thyroid series in contrast to an average weight of 42.8 milligrams in the thyroid-free controls. Histologically the ovaries of the thyroid-fed rats resembled those of immature rats, 20 to 30 days of age. No mature follicles or corpora lutea were present in any of the thyroid-fed rats. However, immature follicles or corpora lutea were numerous and many young follicles undergoing atresia were observed. Moderate degrees of edema were noted in the medullary portion and there was evidence of hematosi in the medullary blood vessels. The germinal epithelium appeared normal. No significant differences were noted between the animals receiving 0.5 or 1.0 per cent of thyroid. In rats maintained on thyroid-free rations the ovaries were normal throughout.

## ESTROGENIC EFFECT IN A 15 YEAR OLD BOY

WENNER (BASEL)

Monatschr. f. Geburtsh. u. Gyn., 119: 168, 1945

The subject of this report was a 15-year-old helper in a chemical laboratory in which stilbestrol was one of the substances worked with. For several days he had complained of an increase in the size of his breasts, a darkening of the nipples and dark pigment formation on the scrotum. He was first examined a week after he had ceased work at the laboratory. Daily doses of perandren were given for 14 days, at the end of which time the breasts had returned to their normal size and the scrotum had become paler. It was found that the boy had not worked with stilbestrol but had handled the related substances 3,4 Di (b-hydrooxy-phenyl)-3,4 dioxihexan and 3,3 Di (b-hydrooxy-phenyl) hexanon 4. It is believed that he inhaled these substances rather than absorbed them percutaneously.

## EFFECTS OF SEX HORMONES ON THE BLOOD IN RATS

V. KORENCHESKY AND K. HALL

J. Endocrinol., 4: 103-108, 1945

From experimentation, the authors present the following conclusions regarding the effects of sex hormones on the blood in rats.

The number of red cells, hemoglobin content, color index, volume of packed cells and mean corpuscular volume were not affected by the sex of the animals, gonadectomy nor by estrus. In 8 senile rats a mild hypochromia was observed. Androgens increased the RBC, hemoglobin content and volume of packed cells in normal senile and castrated adult male rats, the lowered color index of senile rats being raised. Small doses of estradiol benzoate-butyrate injected alone into male or female rats had no effect on the blood values examined. A definite decrease in the RBC, hemoglobin content and volume of packed cells occurred when progesterone and estradiol benzoate-butyrate were injected together into ovariectomized rats. The effect of androgens in castrated rats was neutralized by simultaneous injection of estradiol benzoate-butyrate, but not when thyroid hormone was given in addition to these.

The results are discussed with reference to sex differences in the human blood picture and to the cause of pregnancy anemias. The amount of fat tissue in bone marrow apparently reflects the changes in general fat deposition and not changes in hemopoiesis. These experiments, while showing definite effects of sex hormones on the blood, do not explain whether the results obtained were due to changes in blood volume or in hemopoiesis. 7 references.

THE ROLE OF THYROID GLAND AND OESTROGEN IN THE  
REGULATION OF GONADOTROPHIC ACTIVITY OF THE  
ANTERIOR PITUITARY

J. P. CHU AND S. S. YOU

J. Endocrinol., 4: 115-24, 1945

The authors conclude, as a result of their experiments, that the follicle-stimulating and luteinizing hormones of the pituitary are under the direct regulation of the thyroid gland.

The daily injection of 1 mg. of stilbestrol or estrone into normal intact rabbits caused complete inhibition of ovarian activity for 30 days; the same treatment was found ineffective in thyroidectomized animals even with a longer injection period.

The feeding of small doses of desiccated thyroid to thyroidectomized rabbits prevented hypertrophy of ovarian follicles, while larger doses had an inhibitory

action on the ovary. The results of simultaneous administration of estrogen and desiccated thyroid to thyroidectomized rabbits were the same as those obtained by feeding desiccated thyroid alone.

Small doses of estrogen did not effectively suppress ovarian activity in intact normal rabbits; addition of small amounts of desiccated thyroid reinforced the inhibitory action of estrogen.

Feeding small doses of desiccated thyroid to normal intact rabbits had no effect on the ovary; large doses caused incomplete inhibition of ovarian activity.

The pituitary gland of thyroid-fed normal and thyroidectomized rabbits contained a high concentration of ovulating hormone and that of estrogen-treated animals contained very little. 13 references.

## OVARIAN STIMULATION BY OESTROGENS. 2. STIMULATION IN THE ABSENCE OF HYPOPHYSIS, UTERUS, AND ADRENAL GLANDS

P. C. WILLIAMS

J. Endocrinol., 4: 125-26, 1945

The author describes experiments which show that the adrenals and the uterus are not involved in the stimulation of the ovary by estrogens.

A group of immature female rats was hysterectomized; some were killed and the remainder hypophysectomized. Some of the hypophysectomized rats were given stilbestrol. All were killed 5 days after hypophysectomy. Results showed that hysterectomy alone affects neither the weight of the ovaries nor the fall that normally occurs after hypophysectomy, and that the stilbestrol-injected rats have ovaries significantly heavier than have normal rats. A group of immature female rats was hypophysectomized and adrenalectomized 5 days after removal of their uteri. Half of these were given stilbestrol and all were killed 5 days after hypophysectomy. Results showed no indication that adrenalectomy had interfered with the ovarian stimulation.

The author concludes that there is no evidence that this effect of estrogens is an indirect one. 6 references.

## STUDIES OF THE BIOLOGICAL ACTION OF SERUM GONADOTROPHIN. 1. DECLINE IN OVARIAN RESPONSE AFTER HYPOPHYSECTOMY

P. C. WILLIAMS

J. Endocrinol., 4: 127-30, 1945

A single injection of 70 I.U. of serum gonadotrophin (in the form of reconstituted dried pregnant mares' serum) was given to a group of intact immature

rats and to groups of immature rats hypophysectomized at intervals from 14 days before the injection to 4 days afterwards. The rats were killed 5 days after the injection and the ovaries and uteri examined. A basal condition of ovarian responsiveness was attained 7 days after hypophysectomy. Ovulation occurred in rats injected up to 4 days after operation but not in the rats injected later.

The author discusses briefly the roles of endogenous gonadotrophin and of the initial condition of the ovaries in the ovarian response. 7 references.

## STUDIES OF THE BIOLOGICAL ACTION OF SERUM GONADOTROPHIN. 2. OVARIAN RESPONSE AFTER HYPOPHYSECTOMY AND OESTROGEN TREATMENT

P. C. WILLIAMS

J. Endocrinol., 4: 131-36, 1945

In the present study the author attributes all the qualitative differences between the responses of intact and hypophysectomized rats to serum gonadotrophin to the atrophic condition of the ovaries in the latter animals. He states that some of the quantitative differences are probably due to the same cause.

Single injections of 5-130 I.U. of serum gonadotrophin were made into intact, or hypophysectomized, immature rats, or into immature hypophysectomized rats implanted with stilbestrol. Ovulation and luteinization were produced in the intact rats and stilbestrol-implanted, hypophysectomized rats but not in the unimplanted, hypophysectomized rats. The ovarian weight response to 13-14 I.U. was greatest in the estrogenized, hypophysectomized rats but with higher doses the response in the intact rats was the greatest. 10 references.

## STUDIES OF THE BIOLOGICAL ACTION OF SERUM GONADOTROPHIN. 3. ROLE OF ENDOGENOUS GONADOTROPHIN

P. C. WILLIAMS

J. Endocrinol., 4: 137-42, 1945

The author finds that there is no evidence for an increased secretion of endogenous gonadotrophin following injections of serum gonadotrophin giving responses within the normal physiological range. It is suggested that the response in rats immediately after hypophysectomy is a more accurate indication of the intrinsic activity of injected gonadotrophin than the responses in intact rats or in rats injected when ovarian atrophy has occurred following hypophysectomy.

Doses of 1-650 I.U. of serum gonadotrophin were injected into intact immature female rats and into similar rats 1 hour after hypophysectomy. In the intact rats doses of 13 I.U. were purely follicle-stimulating; ovulation and luteinization were produced with lower or higher doses. The maximum ovarian weight attainable was 180-200 mg. In the hypophysectomized rats the maximum ovarian weight was 100-120 mg. Histologically the ovaries were similar to those of the same weight in the intact rats except that ovulation and luteinization were not obtained with ovaries weighing less than 25 mg. The log. dose-response curves for uterine or ovarian weight are parallel in the two groups.

There was loss of ovarian and uterine weight in the hypophysectomized rats injected with less than 10 I.U. and this dose is therefore regarded as quantitatively equivalent to the normal secretion of endogenous gonadotrophin in 5 days. The ovulation and luteinization produced in intact rats with ovaries of less than 25 mg. must be due to endogenous gonadotrophin; that produced with higher doses in intact and hypophysectomized rats is due to the injected gonadotrophin alone. 7 references.

## PATHOLOGY OF DYSMENORRHEA IN THE VIRGIN AND SPASM OF THE UTERINE ISTHMUS

CLAUDE BÉCLÉRE AND H. SIMONNET

Gynec. Obst., Paris, 44: 79-81, 1944-45

The sexual development of 10 girls and women suffering from dysmenorrhea was studied. At the time of study 8 were between 14 to 22 years of age and two were between 29 and 35 years old. In 60 per cent of the cases puberty had been precocious, with menarche between the ages of 10.5 and 12 years. Breasts were overdeveloped in 40 per cent and normal in 30 per cent. In 60 per cent the breasts had begun development between the ages of 9 and 12.5 years. Pubic hair was overdeveloped in 40 per cent and normal in 50 per cent. The vulva was normal in 50 per cent and overdeveloped in 20 per cent. In 70 per cent the volume of the uterus was normal and in 30 per cent small.

Eight doses of folliculin (400 I.U. or more) were given in six cases about the sixth day before a menstrual period with good effect.

From these observations and a review of clinical, radiological and hormonal studies, it is concluded that dysmenorrhea is produced by spasms of the isthmus uteri. The painful contractions of the muscles of the uterus are provoked by an excess of folliculin. Spasmodic dysmenorrhea will respond to treatment with preparations from hormones of the corpus luteum or male hormones.

(A very definite over-simplification of the etiology as well as the treatment of primary dysmenorrhea.—Ed.)

## THE MENSTRUAL CYCLE

### A FIBRINOLYTIC ENZYME IN MENSTRUATION AND LATE PREGNANCY TOXEMIA

O. WATKINS SMITH AND GEORGE VAN S. SMITH

Science, 102: 253-254, 1945 .

Although the lack of prothrombin and fibrinogen in menstrual discharge has been demonstrated, thus suggesting that the blood in it has been clotted and the clot dissolved, evidence for the existence of lytic substances to account for the fluidity of the discharge has not been conclusive. It has been suggested that the fibrinolytic action in the uterus might be an explanation, and also that a proteolytic enzyme might account for the toxicity of the euglobin fraction of menstrual discharge. Such an enzyme might be a product of endometrial injury due to the withdrawal of hormonal support and the toxic by-product might be the final cause of menstruation through vascular injury. This paper presents the results of studies made to test this theory. Since the hormonal situation in toxemia of late pregnancy is analogous to that existing at the time of menstruation and the vascular changes are similar to the local ones in the menstruating endometrium, sera from patients with late pregnancy toxemia were also tested.

Fibrinolytic activity was tested by the method described by Tagnon, Davidson and Taylor. Fresh plasma from oxylated human venous blood was used as the source of fibrinogen. All 12 specimens of fresh menstrual serum which were examined contained marked fibrinolytic activity. There was evidence that the enzyme was more concentrated in the endometrial debris than in the serum. Ten specimens of venous blood taken from 5 women during menstruation were also consistently fibrinolytic. Seven specimens taken from 4 women during the intermenstruum were entirely negative. The sera from 7 patients with late pregnancy toxemia, 1 with eclampsia, and 1 flowing prior to miscarriage at four months, were all markedly positive for fibrinolytic activity. No enzyme was demonstrated in the eclamptic patient and in the 2 women with toxemia when studied two weeks later after they had been delivered and were well. The sera of 7 normally pregnant women were also negative. The authors conclude that, although the enzyme and toxin are both concentrated in the euglobin fraction of menstrual discharge, they are not identical, for these reasons: (1) the fibrinolytic activity of many venous sera was as great as that in menstrual serum; (2) they were unable to demonstrate toxicity in the venous serum of toxemic or menstruating women; (3) samples of menstrual discharge that have lost toxicity on standing may completely retain their fibrinolytic activity.

A brief report is given of preliminary studies to test the theory that pathological syndromes associated with cellular injury of any cause might be the effect of release of toxic by-products of proteolysis from the action of this enzyme. Of

8 patients with gynecological complaints, the sera of 4 contained fibrinolytic activity before operation. Blood specimens taken from the other 4, whose preoperative tests had been completely negative, all showed fibrinolysis from one to three days after operation.

(It is curious that, in spite of the large number of studies on the subject, going back nearly half a century, the question of the non-coagulability of menstrual blood has not yet been established beyond doubt. Formerly opinion appeared to be divided between those who believed that the body blood, in its passage through the uterine mucosa, was deprived of one of its clotting principles and those who believed that an anti-clotting principle was added. The still earlier view, that the non-coagulability is due to the addition of the alkaline cervical mucus, had long since been disproved. In recent years the concept that a proteolytic factor or enzyme is responsible for the fluidity of the menstrual blood appears to be establishing itself, and evidence on this point was set forth in a paper by Huggins, Vail and Davis in 1943 (*Am. J. Obst. & Gynec.*, 46: 78, 1943). The present paper by Smith and Smith supports this general thesis, the authors suggesting that the enzyme with this fibrinolytic action is a product of endometrial injury due to withdrawal of hormonal support. In a previous paper they had suggested that this toxic principle might be the actual cause of menstrual bleeding. This hypothesis, however, needs further study before it can be accepted, and it is perhaps too early to be sure that the riddle of menstrual non-coagulability has been solved.—Ed.)

## QUANTITY OF MENSTRUAL FLOW

R. A. STEVENSON, JAMES C. STINSON, JR., AND B. AINSWORTH KUEHNE

*Texas Rep. Biol. & Med.*, 3: 371-381, 1945

The subjects of this study were 96 unmarried volunteers from the John Sealy College of Nursing. They ranged in age from 17 to 35 years and all considered themselves normal with respect to their menstrual periods. At the beginning of a period each was given weighed sanitary napkins and a weighed, opaque, air-tight jar. The jar containing the used pads was returned at the end of the period, accompanied by information relative to the duration of the period, pain, etc. Calculations of the blood lost were made by subtracting the weight of the materials issued from that of the materials returned. The study covered a period of six months. The mass of material lost from menstruation was found to vary over a wide range, from 5 to 156 grams, with a mean of 48.5 and a standard deviation of 34.4. Duration of the flow in individual subjects was relatively constant, but mass of flow showed some fluctuation from month to month in a given subject and was reflected roughly in the variable number of pads used. Correlation between duration of flow and mass of flow was found to be negligible except in a few extreme cases. Clots were reported by 46 per cent of the subjects; 36 per cent reported no clots; and 16 per cent did not reply on this question. No correlation was noted between the occurrence of clots and dysmenorrhea. Dysmenorrhea was reported by 60.5 per cent. None of the subjects reported

the occurrence of pain during and after bleeding only. No correlation was noted between the severity of dysmenorrhea, amount of flow, age of subject or any combination of these three factors. Bleeding began in the morning in 58 per cent, in the afternoon in 19 per cent and during the night in 22 per cent. The time of onset in successive periods of a given subject was fairly constant. The sources of error existing in this study include urination, loss prior to donning pad, bathing, feces on the pad, and evaporation.

(This interesting study was carried out by a method which is handicapped by certain sources of error, though these are fairly stated by the authors themselves. A favorite method for studying blood loss at menstruation has been to determine the amount of hemoglobin in the blood of the menstrual napkins, since hemoglobin constitutes a definite and known proportion of the total weight of the blood. Others have studied the blood loss more directly by the employment of cup-like receptacles applied intravaginally. Although there are wide individual differences, there is still considerable divergence of opinion as to what might be called an average blood loss.

A number of other side-lights of the study are of interest, such as the incidence of clotting. A good many of our patients are unduly apprehensive when clots appear in the flow, and yet the authors reported that this occurred in 48 per cent of their ostensibly normal group. Whatever the mechanism of the nonclotting characteristics of menstrual blood may be, it is certainly often impaired, especially when the menstrual amount is large, and this without any serious significance in itself.—Ed.)

## ANDROGEN THERAPY OF MENOPAUSAL SYMPTOMS IN CANCER PATIENTS

S. B. GUSBERG

Am. J. Obst. & Gynec., 50: 502-508, 1945

The author has become dissatisfied with the use of stilbestrol in a certain group of menopausal patients in whom he believed the stimulating effect of estrogen was contraindicated. This includes those who have been treated for some form of cancer of the reproductive organs and also those in whom estrogenic therapy has provoked uterine bleeding. This has led him to the use of androgen therapy in a selected group of menopausal patients. The course of treatment which was found most effective was 20 mg. of methyl testosterone by mouth daily for 4 weeks, then 10 mg. daily for 2 weeks thereafter. He usually allows several intervals of 1 week without treatment during the course.

Of 24 symptomatic menopausal patients, 23 were strikingly benefited by androgen therapy. For those patients whose menopause was recent, results were excellent and uniform. The outcome was less striking in late cases but some benefit was received. There was possible slight hirsutism in 2 cases. Of 12 patients who had had previous stilbestrol therapy, 10 were benefited to a greater degree by the androgens.

In view of his experience the author believes that the use of the androgens rather than estrogens is indicated in the following groups: (a) Patients who have been treated for cancer of the reproductive tract or breast. (b) Patients who have been treated for abnormal bleeding during the climacteric. (c) Patients who have developed uterine bleeding while under treatment with estrogenic substances. (d) Patients who require endocrine therapy for vasomotor symptoms before their menses have completely ceased. (e) Patients who have been addicted to stilbestrol by long-continued usage.

(For the treatment of menopausal symptoms, when organotherapy seems called for, testosterone usually offers no especial advantage over the estrogens. However, for the groups enumerated by the author, it is often preferable. With either testosterone or estrogen, the oral route of administration is always to be preferred. There is rarely any need nowadays, for this indication, to resort to the "shot" treatments formerly so popular.—Ed.)

#### THE DIFFERENTIAL DIAGNOSIS OF GYNECOLOGICAL BLEEDING WITH PARTICULAR REFERENCE TO ENDOMETRIAL HYPERPLASIA, BASED ON THE MATERIAL OF THE BASEL UNIVERSITY WOMAN'S CLINIC, 1935-1939

Inaug. Disser. Medical Faculty, Univ. of Basel, 1944; p. 41

The material investigated in this study comprises the cases of hyperplasias of the endometrium treated at the Woman's Clinic in Basel in the years 1935-1939. There were 205 cases, including 198 curettings. The clinical diagnosis in the latter 198 cases was confirmed histologically. The noncuretted cases included juvenile bleedings in which a histological study was superfluous and a case of secondary anemia, the diagnosis of which was confirmed by the results of treatment.

The greatest number of patients (63) were between the ages of 46 and 50 years. Twelve patients were in the age group 13 to 20 years, inclusive.

More than half of the patients gave a history of altered periods before the beginning of the pathological bleeding. Sixteen women had amenorrhea of some duration, in some cases due to suspected menopause and in some to pregnancy. In 33 cases the abnormal bleeding began before the eleventh day after cessation of the last period. According to Schröder's observations, this is due to endometrial necrosis consequent upon persistence of follicles. In most cases, however, the abnormal bleeding was preceded by an amenorrhea of more than four weeks.

The findings at palpation were as a rule normal; in 51 cases the uterus was definitely enlarged or only somewhat plump. Unilateral enlargement of the adnexa was noted in 22 cases. The pathological bleedings in this group of women ranged from a few days and weeks to months and years.

In the majority of cases the pathological-anatomical diagnosis was glandular-cystic hyperplasia. There were encountered also in combination with endometritis, adenomyomatosis, disturbances of the circulation, tuberculosis of the mucous membranes, precancerous changes and polyposis.

In addition to the histologically confirmed cases of glandular-cystic hyperplasia, the number of relapses was of interest. In 21 cases a relapse was confirmed by a second histological examination. In 32 cases the diagnosis of the relapse was clinically certain and in 58 cases it was probable on the basis of the history.

## VULVA AND VAGINA

### LACTOBACILLUS THERAPY IN VAGINITIS DUE TO TRICHOMONAS

LEO BRADY AND ROGER D. REID

Am. J. Obst. & Gynec., 50: 509-513, 1945

The authors recall that the rationale for the use of lactobacillus therapy in vaginitis due to trichomonas is two-fold: (1) live, lactic acid-forming bacilli, one million per tablet, provide for a pH maintenance of about 5.5; (2) lactose is furnished to ensure adequate growth and activity of the Döderlein bacilli.

This is the authors' second report of their results with lactobacillus therapy in trichomonas vaginitis and is based on 70 cases. All patients complained of leucorrhea and half of pruritus. Dyspareunia was the outstanding complaint of 15.

The method the authors advise at the present time is the following: As soon as the diagnosis is made, a bivalve speculum is introduced into the vagina, the cervix inspected for complicating endocervicitis, and Skene's and Bartholin's glands inspected for possible involvement. The vagina is then dried with cotton and two lactobacillus tablets inserted high in the vagina in the posterior fornix behind the cervix. The vaginal orifice is then plugged with a tampon of non-absorbent cotton. When the patient returns on the next day, the tampon is removed, material taken from the vagina for microscopic study, and the treatment carried out on the preceding day is repeated. On this second visit practically every patient will report that the itching has become much less, and it is very unusual to be able to demonstrate organisms at this time.

Such office treatments are repeated daily for five days. The patient is then told to insert two lactobacillus tablets high in the vagina each night. She is told to take douches only if she becomes uncomfortable from unabsorbed particles of the tablets coming out of the vagina and causing irritation. If a douche is used, white vinegar (5 per cent acetic acid) is recommended in a strength of from 2 to 4 tablespoonfuls to 2 quarts of water. Two douches a week are usually sufficient.

This home treatment is continued from two to four weeks and longer if necessary. However, if the organisms promptly disappear and show no immediate tendency to recur, the tablets need be used only every other night. It is especially important that they be used while the patient is menstruating, as that is, of course, the time when the vaginal defenses against the trichomonads are weakest. In a few instances the authors had the patient return for a second course of five-day treatments in the office, but this is rarely necessary.

Wet preparations taken after 2 weeks of treatment were negative in 64 of the 70 cases and all but 3 of the patients stated that their symptoms had disappeared.

(In a previous paper (Ann. Surg. 115: 840, 1942) the authors had made a preliminary report on this method of treating trichomonas vaginitis, and the present paper based on the study of 70 additional cases, appears to justify their enthusiasm for the method. The principles on which it is based, as explained in the paper, make this plan of therapy seem very rational. At any rate, any addition to our armamentarium in the treatment of this troublesome disorder will probably be welcomed by many.—Ed.)

## SWEAT GLAND TUMORS OF THE VULVA, BENIGN (HIDRADENOMA) AND MALIGNANT (ADENOCARCINOMA)

EMIL NOVAK AND R. R. STEVENSON

Am. J. Obst. & Gynec., 50: 641-659, 1945

This paper is based on the study of 15 cases of benign sweat gland tumors (hidradenoma) and 2 malignant tumors thought to be of sweat gland origin. The literature is first reviewed, after which the authors discuss the various types of sweat glands found in the body, as well as their distribution in various regions.

The sweat gland tumors of the vulva constitute a relatively rare but highly interesting group. Clinically they present as small and innocent-looking growths on or near the vulva, but to one not familiar with their histological appearance the microscopic picture is apt to be rather startling, and perhaps to lead to the diagnosis of adenocarcinoma. However, in only one case in the literature, that of Eichenberg, has there been apparently unimpeachable evidence of malignant change, both clinical and microscopic. All other cases, including the 15 cases reported herewith, have been clinically benign and all have been cured by simple excision.

Granted that the characteristic microscopic picture of these growths might well in other tissues lead to the diagnosis of adenocarcinoma, there would seem to be no justification for applying the term adenocarcinoma to these notoriously benign sweat gland tumors. It is entirely possible, and perhaps even probable, that some instances of the rare primary adenocarcinoma of the vulva may be of sweat gland origin, as in the two cases of this group which have been included in this paper. Such an origin, however, is difficult to establish. The histogenesis of these sweat gland tumors has been thoroughly discussed in the paper, and the suggestion made that the apocrine gland derivation of these growths has probably been overaccentuated, though our knowledge on this point is still very incomplete. The clinical and microscopic characteristics of hidradenoma have likewise been rather fully discussed in the paper.

## THE UTERUS

### THE PATHOGENESIS OF POSTSALPINGECTOMY ENDOMETRIOSIS IN LAPAROTOMY SCARS

JOHN A. SAMPSON

*Am. J. Obst. & Gynec.*, 50: 597-620, 1945

The author's experience as well as that of others has shown positively that scar endometriosis can arise from normally situated uterine and tubal mucosa by continuous invasion. The very strong circumstantial evidence that it also arises from the transplantation of bits of uterine mucosa in the abdominal wound during hysterotomy for the termination of early pregnancy has greatly strengthened the possibility of the transplantation and growth of this mucosa in the abdominal wound during other pelvic operations. A large number of these cases have followed salpingectomy or tubal sterilization combined with ventrofixation of the uterus. This type of operative procedure should create conditions favorable not only for the continuous invasion of the abdominal scar by tubal or uterine mucosa, but also for the growth of bits of these mucosae transplanted in this operative field.

Seventeen cases of laparotomy scar endometriosis, with photomicrographs are reported. The first operation, in all but one case, consisted of bilateral salpingectomy or tubal sterilization followed by intentional or accidental ventrofixation of the uterus. In the one case in which salpingectomy had not been done, the scar endometriosis followed a myomectomy. Endometriosis was found about the tubal stumps in the 13 uterine cornua which were adherent to the scar endometriosis as well as in a cornu not in actual contact with the scar but connected to it by a long drainage tract. The author found that scar endometriosis was derived from the mucosa of a tubal stump by continuous invasion in 10 specimens. Transplantation endometriosis was possibly present in three scars.

Injection of the uterine cavity with colored gelatin was very helpful in the study of these cases. In the 12 cases in which this was done, the gelatin was found in the scar endometriosis in 8, thus demonstrating the continuity of the scar with the uterine cavity. In one case the tubules of the scar contained gelatin although the only contact with the uterus was the remains of a drainage tract 7 cm. long.

An interesting feature of postsalpingectomy endometriosis is that the ectopic mucosa, which can be shown to have had its origin in the mucosa of a tubal stump and to have grown from it by continuous invasion, may not only retain the structure of the tubal mucosa, but may also assume both the structure and function of the uterine mucosa, including its reaction to menstruation and pregnancy, thus producing a true endometriosis. Even the endometriosis derived from the stump of the isthmus of the tube may be of uterine type. Mucosa of

uterine type was present in the scars of all specimens of postsalpingectomy scar endometriosis studied by the author.

(It is just about a quarter of a century since the publication of the first of the classical series of papers by Sampson on endometriosis, and the present paper shows that throughout all these years he has maintained his interest in this subject. His work in this field is undoubtedly one of the most important contributions of our time, and the disease which he so fully described in his earliest papers is now universally recognized, and will always be associated with his name. Although eponymic designations are now frowned upon, there would seem to be ample justification for calling it Sampson's disease.

Another thing demonstrated by this paper is the thoroughness and completeness of study which has been a feature of every publication of Sampson on this subject. While for the group of cases comprised in the present study, those of postsalpingectomy type, few would take issue with his conclusions, his method of gelatin injection makes all the more convincing his contention that the endometrium of the abdominal scar is directly traceable to the stump of the tube. Even without the gelatin injection, this point would probably be readily enough conceded on the basis of the histologic study itself, especially in view of Sampson's own previous studies showing that endometriosis may arise from the stumps of amputated tubes.

However, this paper does not touch upon, nor does it seem to explain, the cases of laparotomy scar endometriosis which have occurred following operations in which there has been no conceivable invasion of either the uterine or tubal lumina, and it is this group which has been the source of the greatest contention between those advocating the implantation explanation and the proponents of the so-called celomic metaplasia theory.—Ed.)

## ENDOMETRIOSIS

ALVIN O. SEVERANCE

Texas State J. Med., 51: 310-312, 1945

This paper begins with a brief discussion of the various theories which have been advanced to explain the etiology of endometriosis (Cullen, Sampson, Meyer, Novak, and Halban). A review is given of the symptoms, treatment and mortality figures in 569 cases reported by Haydon, and data on the incidence of endometriosis reported by various workers are tabulated. The author's original data include a table showing the distribution of cases of endometriosis treated at Nix Hospital, 1942-1944, inclusive, by site of the endometriosis. The uterus was the organ most frequently attacked in this series of cases (186 out of 278 total cases). Endometriosis of the ovary occurred in 62 cases. There were 9 cases of endometriosis of the tubes, 7 of the appendix, 5 of the cervix, 3 each of the vagina and peritoneum, and 1 each of the rectum, colon and abdominal wall. Another table presents statistics of surgical specimens examined in the same hospital over the same period of time. In 1942 endometriosis was the diagnosis made in 16 per cent of the gynecological specimens. Corresponding percentages in 1943 and 1944 were, respectively, 24 and 14.

THE VALUE OF THE VAGINAL SMEAR IN THE DIAGNOSIS OF  
UTERINE CANCERJOE V. MEIGS, RUTH M. GRAHAM, MAURICE FREMONT-SMITH, LOIS T. JANZEN,  
AND CAREY B. NELSON

Surg., Gynec. &amp; Obst., 81: 337-345, 1945

The authors feel that the vaginal smear technique for diagnosis of uterine malignancy is a definite step forward in the early recognition of the disease.

A series of 1015 cases is presented which were studied by vaginal smear with a diagnostic error of 4.0 per cent. Of a total of 154 positive cases (39 endometrial and 109 cervical cancer) 16 were incorrectly called negative by vaginal smear. Seven of these errors were due to failure to examine every field of the slide. In the other 9 cases, no evidence of cancer cells ever was found, supposedly because either the malignant cells did not exfoliate or they degenerated. Cells from endometrial carcinoma frequently fail to appear in the vaginal secretion.

The criteria for recognition of cancer cells in the vaginal secretion are briefly as follows: (1) the basal cells, varying in size, round or oval with green cytoplasm and an active vesicular nucleus; (2) precornified cells, larger, more transparent and having a smaller vesicular nucleus; (3) cornified cells, similar to precornified except for an acidophilic cytoplasm and pyknotic nucleus; and (4) occasionally encountered very small endometrial cells.

In reviewing the errors in the group "negative called positive" the authors found that certain cells, probably histiocytes, often were misleading, being mistaken for malignant cells. One example of this is the foreign body giant cell. Normal endometrial cells may also be mistaken for cancer cells because their nuclei are hyperchromatic and there is very little cytoplasm. Another type of cell which caused some confusion is the atrophic cell of the basal layer of the vagina. The authors' solution for this problem was to change the vaginal epithelium from atrophic to cornified by the administration of stilbestrol.

For the diagnosis of uterine cancer, inspection and palpation have been found to have obvious limitations. For this reason, various aids have been suggested for earlier diagnosis. Schiller's test is one of these. The cervix is painted with iodine, the normal tissue staining deeply, cancer cells staining very lightly or not at all. This test can be confusing since erosions and inflammations also take the stain to a limited degree. The value of the Schiller test is that it indicates those portions of the cervix from which biopsy material should be taken. Another proposed method for early diagnosis is the colposcope but this is found unpracticable for examining large numbers of women because of the gynecologist's unfamiliarity with the magnified cervix.

The vaginal smear is of value because it can be accomplished easily and is an accurate means of establishing early diagnosis. However, it should be used in conjunction with the biopsy, which is the most important method. Vaginal

smear and biopsy are complementary techniques. The most important contribution of the vaginal smear technique may be in cancer control. Large numbers of women may be screened and those with positive smears studied further by biopsy. The authors do not regard a negative smear as excluding cancer; nor a positive smear, without biopsy confirmation, as an indication for surgery.

Abstracts of 8 cases, diagnosed primarily by vaginal smear, are presented to illustrate the value of the vaginal smear in the early diagnosis of cancer. 5 references. 8 figures.

(The vaginal smear method for the diagnosis of uterine cancer was commented upon rather fully in connection with the article by Gates and Warren, abstracted in the February issue of the Survey. To this the reader may be referred. In the latter article the authors mentioned that in many cases they had obtained very satisfactory results from the employment of the simple hematoxylin-eosin method of staining, rather than the more complicated Schorr technique employed by Meigs and his co-workers. This statement I can endorse on the basis of a small group of cases in which I have employed the simpler method since the appearance of the paper by Gates and Warren. It would seem, as was stated in my previous comment, that the chief value of the vaginal smear technique would be as a screening test in the study of large groups of women, but that it can scarcely be expected to replace biopsy and diagnostic curettage in the decisive diagnosis of uterine cancer.—Ed.)

## PRINCIPLES OF TREATMENT OF CARCINOMA CERVIX UTERI BY RADIOTHERAPY

BERNARD SANDLER

Proc. Roy. Soc. Med. (Sect. Obst. & Gyn.), 38: 175-183, 1945

There is experimental evidence that with a relatively small dose of irradiation the death of the cell is brought about by the damage sustained during the resting stage in the nucleus, particularly to the chromosome. This damage is due to direct ionization, and it is observed in the next mitosis when there are broken chromosome and chromosome fragments present in the dividing cell. The daughter cells, being deficient in their nuclear contents, will die. The damage to the nucleus of the cell resulting in this death is a direct radiation effect. If several adjacent cells die simultaneously after a much larger dosage, there will be a change in the histological organization of the tumor tissue; any local failure in blood supply will cause a breakdown of a still larger cell population.

With the breakup of the tumor parenchyma by cell degeneration, the response of the tumor bed (that is, the indirect effect of the radiation) comes into play. Infiltration and subsequent differentiation of cells of the reticulo-endothelial system (plasmocytes, histiocytes, lymphocytes and cells of the granulocytic series) form part of the repair process. The problem is how to control both the intracellular radiation effects and the intercellular response. If cells are killed rapidly and in too great a number or if the tumor bed is damaged the repair

process will be unable to function properly and fibrosis may occur prematurely. Cytological analysis of the radiation effects is of the utmost importance especially at the stage when the intra- and intercellular processes are in progress, if we are to assess the degree of the biological response of the tumor and control the treatment.

In a series of cases of squamous carcinoma of the cervix the author delivered to each case exactly 100 R by x-ray and 24 hours later took pieces of tissue for biopsy. Although the tumors were histologically similar, great variation was observed in the response; in one case only 5 per cent and in another 45 per cent of the dividing cells showed radiation-induced chromosome abnormalities. Since the ultimate death of the tumor depends upon the production of these abnormalities and the frequency of cells effected, clearly a different type of treatment will be required for any two tumors showing so wide a variation in cytological response. It would seem illogical to give the same dose to each of them, yet that is what happens so frequently with the standard techniques in use today.

To the question "What is a lethal dose?" there can be therefore no fixed and simple answer applicable to all tumors of a given organ or tissue as assumed by some workers. Control of the intracellular and of the intercellular effects of radiation during treatment is desirable and the cytological findings suggest that much of the radiation given at present may either be wasted, because it is delivered without regard to the biological behavior of the tumor cells, or may be actually harmful and damage the repair process. It is possible that cytological research can provide a more scientific basis for a treatment plan in carcinoma of the cervix to replace the empiricism upon which dosage has been administered so far. There would appear to be then a very strong case for a reorientation of our ideas on dose fractionation and total dose. This can be obtained only from cytological research.

In discussing certain physical problems the author notes that even in the early stages, spread to the lymph nodes of the lateral pelvic wall may have taken place while the growth is apparently still confined to the cervix. The frequency of such invasion in stages 1 and 2 may be as high as 40 per cent. One must therefore contemplate treating the whole of the true pelvis, and even this may be too small a volume to include all the main sites of invasion, since many patients have involvement of lymph nodes extending above the brim. Although it is often asserted that the level of the iliac nodes is at the bifurcation of the iliac vessels—in turn said to be at the level of the pelvic brim—it is not uncommon to find both the bifurcation and the invaded nodes above the level of the brim. Clearly then, the volume to be treated must be not less than the true pelvis and should in many cases include more than that volume.

In discussing dosage the author notes that in the uterus variations in length, the presence of fibroids, distortion by the carcinoma itself, lateral deviation, acute anteversion or retroversion will effect the dose delivered. In the vagina the variations depend among other things on the size, shape, and distensibility of the vaginal vault and are not related in this respect to the stage of the disease. These physical dimensions, therefore, have a primary determining influence on positions of the applicators and consequently on the lethal "isodose" surface

produced. This influence may be much greater in some cases than that of the type of technique used in the particular size of vagina under consideration.

Alterations in the relative positions of the organs in the pelvis during or after treatment are frequent. Some of the more important of these factors which cause an alteration in the relative position of the organs may be: (a) the presence or absence of packing, the degree of distension of the bladder and rectum and the posture of the patient. (b) Regression of a large tumor or stenosis of a large cavity in the interval between x-ray and radium therapy will distort the organs and render them unreliable for measurement of the position of the radium. (c) Mechanical faults occur due to slipping of applicators. By a special apparatus the position of the radium in situ in the bony pelvis may be recorded. In a series of 30 cases the cervix was found to be pushed in a cephalic direction by the packing to an average of 4 cm. above the level of the symphysis—the usual level given in textbooks.

The fullest cooperation between the gynecologist and x-ray therapist should be undertaken before any treatment is given. The latter should certainly study gynecology and it is not too much to say that all who handle radium should know something of the physics and biological actions of radiation and of the dangers both to the patient and to the operator.

Before the insertion of the radium every means must be taken to ascertain the limits of the primary and the extent of the spread by palpation, colposcopy, cystoscopy, proctoscopy and pyelography. These five procedures should be routine. Both therapists and gynecologists should be present or have made available to them the results of these examinations.

After a full clinical assessment of the patient the treatment plan must be decided upon. It has been our practice, if the tumor is very large, to give a portion of the x-ray dosage first, in order to produce partial regression of the tumor. This permits later on a much better radium distribution than would have been possible with a bulky tumor filling the vaginal vault. Sometimes direct application by contact x-ray per vaginam has been attempted for this purpose also. Questions of this type must be decided at a joint consultation before any treatment is given. Such questions as lymphadenectomy after radiation should also be decided at that time. The radium having been inserted, 2-plane x-ray photographs should be taken to check the correctness of the insertion and as a record for dose estimation. It will already have been decided by joint discussion what type of applicators to use and the dose to be given.

Variations in the positions of the radium during treatment must be investigated and the dose distribution analyzed. This may require the services of full-time technicians. Since physicists are employed by most hospitals to check the dose distributions of radium applicators used for other organs of the body there is no reason why such work should not be extended to the cervix.

Serial biopsies for cytological analysis and guidance for dosage should be undertaken in cooperation with a cytologist.

(While this article is not a very long one, it has been abstracted rather fully because it embraces a study of the mechanism of radiotherapy in cancer, and because it emphasizes many fine points of therapeutic technique which are not likely to be thought of by the

average gynecologist and probably not by all radiologists. The article is accompanied by 10 illustrations, 4 of which show the effects of radiotherapy upon the chromosomal structure of the cancer nuclei. However, the author emphasizes that one must also take cognizance of the effects produced upon the intercellular tissues. His discussion makes it clear that simple standardization of dosage and technique will often be inadequate in the management of the individual case. What a far cry this represents from the not very remote day when untrained clinicians were wont to employ their "rental" radium so promiscuously, with perhaps only a few simple directions from the radium concern.

The author puts his finger on a vital point of the cancer problem when he states that even in the early stages the cancer may already have spread to the lymph nodes, and he believes that such invasion may occur in as many as 40 per cent of cases in stages 1 and 2. It is this often early dissemination, rather than the primary site, which makes the treatment of cervical cancer the formidable and disappointing problem which it is. The author wisely urges the fullest cooperation between the gynecologist and the radiologist, and emphasizes that everyone who handles radium should know something of its physics and its biological effects, as well as of its dangers to both the patient and the operator.—Ed.)

## THE TREATMENT OF CARCINOMA OF THE CERVIX BY INTERSTITIAL RADIUM NEEDLES AT THE RHODE ISLAND HOSPITAL (SUPPLEMENTAL REPORT)

GEORGE W. WATERMAN AND RALPH DIHONE

*Am. J. Obst. & Gynec.*, 50: 482-488, 1945

This paper is a sequel to one published by the authors in 1937 and adduces additional evidence to show that interstitial radiation by means of low intensity, long needles with 0.5 millimeter platinum infiltration well distributed out in the paracervical and parametrial tissues, has a distinct value in the treatment of cervical cancer and that the results have been achieved without undue immediate mortality or without increasing the incidence of fistula formation. Their plan, in the main, has been to place from 3 milligram needles out into the tissues at the sides of the uterus, 2 needles on each side; they then thrust 2 milligram needles at 1 or 2 cm. intervals in front of and in back of the cervix using in all from 6 to 16 needles. In addition, a 20 milligram intrauterine capsule was employed. The

TABLE 1  
1926-1933, 309 Cases. Survival Rate by Years 1 to 10

STAGE	(SCHMITZ)	NO. CASES	5 YR.	SURVIVAL PER CENT	10 YR.	SURVIVAL PER CENT
	<i>per cent</i>					
I	(4.8)	15	(11)	73.0	(7)	46.0
II	(31.7)	98	(53)	54.0	(39)	40.0
III	(35.6)	110	(36)	32.0	(23)	21.0
IV	(27.9)	86	(0)	0.0		
Composite (100.0%).....		309	(100)	32.3	(69)	22.3
Relative.....		281	(100)	35.7	(69)	24.5

authors' plan of individualizing cases reflects itself in a wide variation in dosage used but they are inclined to regard a dosage of between 5000 and 7000 mg. hours as optimal for the Stage II (Schmitz) tumor and between 4000 and 6000 mg. hours for the Stage III carcinomas. The above technique was supplemented by x-ray therapy in over half of the cases.

The results are summarized in Tables 1 and 4 from this paper. There has been no immediate mortality from interstitial radiation since 1937 in a total of 353 cases treated to January 1, 1945.

In the authors' last 177 cases, there were 21 bladder injuries (11.8 per cent), including 10 vesicovaginal fistulas, and 34 injuries of the intestinal tract (13.5 per cent), including 9 rectovaginal fistulas.

TABLE 4  
1926-1938, 507 Cases. Survival Rate by Years 1 to 5

STAGE	(SCHMITZ)	NO. CASES	1 YR.	2 YR.	3 YR.	4 YR.	5 YR.	5 YR. PER CENT
	<i>per cent</i>							
I	(3.9)	20	20	19	18	16	15	75.0
II	(30.8)	156	140	113	103	99	91	58.4
III	(41.0)	208	150	103	76	61	57	27.4
IV	(24.3)	123	22	8	6	3	3	2.4
Absolute 100%.....		507	332	243	203	179	166	32.7
Not treated (9.7%).....		49					1	
Relative (90.3%).....		458					165	36.0

# DIE ABSOLUTE HEILUNG DER COLLUMKARZINOME UND IHRE BEZIEHUNG ZUR MORPHOLOGIE DES KARZINOMS CARL LAUTERWEIN

Zentralbl. f. Gynäk., 68: 353-359, 1944

This paper gives an analysis of the 3593 cases of carcinoma of the cervix treated in the period 1923-1937 by W. Stoeckel in Kiel, Leipzig and Berlin. In the years 1910-1916, 69.4 per cent of the patients were subjected to the radical operation; in 1917-1922, 42.1 per cent; in 1923-1926, 36.2 per cent; and in 1927-1937, 30 per cent. In the total series there were 1145 five-year cures. This good result is partly attributable to the fact that 55.8 per cent of the carcinomas belonged to groups 1 and 2. From an analysis of the histological findings the author concludes that the time factor should be given greater consideration in radiation therapy. Unripe squamous epithelial carcinomas were found to respond better to radiation from one side. For medium ripe forms radium application from two sides gave the best results and ripe squamous epithelial types responded best to radiation from three sides. Small, fibrous, ascirrhotic squamous epithelial carcinomas were found to respond better to operation than to radiation.

(The analysis of this large number of cases of cervical cases shows an excellent yield of 5 year cures, better than that reported by most workers in the field. This is undoubtedly to be explained by the surprisingly large proportion of Group 1 and Group 2 cases included in the series (58.8 per cent). Interesting, too, is the steady drop in the percentage of patients subjected to radical operation after the introduction of radium. The series includes cases only up to 1937, and it is probable that the figures beyond that year, if they ever become available, will show a still greater drop in the operative incidence.—Ed.)

## CARCINOMA OF THE BODY OF THE UTERUS

LOUIS J. LEVINSON AND WILLIAM BRAMS

J. M. Soc. New Jersey, 42: 320-321, 1945

To illustrate choice of treatment based on the type of carcinoma and age and condition of the patient, three case reports are presented. The first patient, a very obese, 63-year-old woman, had a relatively benign type classified as adenoma malignum which could have been cured by either operation or radiation. Because of the patient's extreme obesity, age, and apparently damaged heart, radium therapy alone was considered the safest method of treatment. A total dose of 4,200 mghrs. was given. During three years of follow-up she has had no bleeding or discharge. The second patient had a highly malignant, very radio-sensitive, anaplastic type of carcinoma. Because of the poor physical condition of this 62-year-old patient, preliminary radium treatment with a total dosage of 5,000 mghrs. followed by vaginal hysterectomy five months later was chosen. She made an uneventful recovery. The third patient, a married nullipara, aged 32 years, had a definite adenocarcinoma. In this case radium therapy (4,000 mghrs.) was followed five weeks later by a panhysterectomy. In all three cases diagnosis had been made from examination of curettings. In spite of the differences in the histological appearances of the carcinomas, their response to radium therapy appeared to be the same. In each case careful examination of the uterus revealed no evidence of residual carcinoma.

(All three of these patients seem to have been well handled, and yet the plans of treatment differed in all three. This illustrates the importance of individualization in the management, not only of adenocarcinoma of the corpus, but in carcinoma of the cervix as well.—Ed.)

## LEIOMYOSARCOMA OF THE UTERUS WITH METASTASIS TO THE FEMUR. REPORT OF A CASE AND REVIEW OF THE LITERATURE

WALLACE S. BROOKE AND J. R. THOMASON

Arch. Surg., 51: 120-124, 1945

A review of the literature revealed only three cases of uterine sarcoma with metastasis to bone (humerus, one case, and spine, two cases). The present re-

port deals with a white woman, aged 43 years, who was admitted to the Salt Lake County Hospital in March, 1944, with the complaint of pain in the left hip of eight weeks' duration. In September, 1939, in another hospital, a spindle cell sarcoma of the uterus had been removed at subtotal hysterectomy with unilateral salpingectomy and bilateral partial oophorectomy. In July, 1943, she consulted a physician for pain in the left knee when she stood or walked. Roentgenograms taken by the physician show an abnormal process consisting of diffuse erosion of the head of the femur, especially in the neck. The patient failed to return to the physician but consulted a chiropractor for treatment. The pain, however, continued in about the same intensity until the middle of January when she was unable to get out of bed because of severe pain in the left hip. She was admitted to another hospital, at which roentgenological examination showed a fracture of the neck of the left femur which was thought to be pathologic. Her leg was placed in a hip spica plaster cast. Eight weeks later she was admitted to the Salt Lake County Hospital. A biopsy of the femur at the fracture site was made. The sections showed interlacing bundles of spindle-shaped cells resembling smooth muscle cells and little intercellular substance. The biopsy wound became infected, progressive damage and destruction of the head and neck of the femur were noted roentgenologically, and a large severe decubitus ulcer developed over the sacrum. She died in July. At autopsy a large, grayish white, moderately firm mass of tissue was found in the region of the upper shaft of the left femur, and extending in the pelvis and up along the spine to the upper part of the abdomen. Microscopic sections from the cervix, the abdominal tumor mass and the left femur showed a spindle cell leiomyosarcoma. A diagnosis of leiomyosarcoma of the uterus with extension to the pelvis, abdomen and left femur was made.

### "HERNIAS OF THE PELVIC FLOOR" VERSUS "PROLAPSE OF THE UTERUS OR/AND RECTUM. A PROBLEM OF NOMENCLATURE, PATHOLOGY AND TREATMENT

CHANNING W. BARRETT

J. Internat. Coll. Surgeons, 8: 242-256, 1945

The author argues that the use of the terms "prolapse" and "proidentia" to designate weakness of the abdominal wall and visceral protrusion in the caudal region is meaningless and misleading since the conditions are the same as apply to defects which, when they occur in the cephalad, ventral, lateral or dorsal portions of the abdominal wall, are recognized as hernias. He, therefore, proposes the use of the word "hernia" for certain conditions in the caudal region. Such hernias present these points: (1) Impairment of the pelvic floor exists; (2) The herniated structures have undergone pathologic change; (3) There is disunion of the normal attachments between the supporting structures and the structure to be supported; (4) Cystocele, rectocele, colpocele, uterocele and

enterocele do not become hernias by bulging into the vagina or rectum, or even essentially by protruding of the vagina or rectum; rather they become hernias if and when they bulge through the musculofascial openings in the pelvic floor.

The treatment for these conditions should be hernioplastic. Because the supporting structures which must be reconstructed also have charge of the functions and timing of reproduction, this sometimes becomes a more difficult and complicated procedure than that employed for other types of hernia. The herniated structures must be returned to the abdomen or be removed, depending upon the pathological changes they may carry. If the uterus is to be retained, every effort should be made to leave it in a normal, uncramped position. If it is removed, attachment of the vagina to the supporting structures should be insured. As visceral support is to be obtained not only by continuity of the pelvic floor but also by the restoration of the normal relations of the uterus and vagina, the vagina should be left in an oblique position, running from the introitus backward and upward close to the hollow of the sacrum, and the uterus should be left in the horizontal position, with fundus forward and cervix backward, this oblique and right angle course being a part of the principle of pelvic floor support. Rebuilding of the pelvic floor consists of: (1) raising the vaginal flap well above the pelvic floor muscles; (2) narrowing the rectal fascia and bringing the separated pelvic floor muscles and fasciae together enough to close the hernial opening but leaving a sufficient pelvic floor opening to allow passage of the vaginal tract, and going back far enough to insure a good grasp of the rectum by the pubo-rectalis; and (3) rebuilding the sphincter ani muscles and the rectovaginal septum if they are not intact. Occasionally there is extensive rectal herniation in addition to herniation through the genital tract. In some of these cases the two conditions may be dealt with at the same time; in others it seems best to deal with the most extensive and urgent condition first. The author's procedure for intrasphincterian hernioplasty begins with a severing of the lower end of the bowel from the skin just inside of the sphincter ani; the bowel is then drawn down, and the pelvic floor is sutured through the greatly dilated sphincter. The enlarged pelvic floor opening is then lessened in size by the placement of two or three sutures in the borders of this opening anterior and posterior to the rectum, after which two or three sutures are placed in the skin and sphincter ani anterior and posterior to the bowel, bringing the new anal opening down to a normal size.

(The author, who is a well-known gynecologist of long experience, includes in his paper many instructive comments on the mechanism of "prolapse." He objects to the latter term, and advances good arguments why visceral protrusions through the vagina should be recognized as hernias. In spite of the justice of his argument it is quite certain that his cause is a lost one in so far as nomenclature is concerned, for such designations as prolapse and procidentia are too well entrenched to be dislodged. One might just as well try to expunge the term "fibroids" as applied to uterine myomas.—Ed.)

## THE ADNEXA

### THE CURABILITY OF GRANULOSA CELL TUMORS

G. E. SEEGER JONES AND R. W. TELINDE

Am. J. Obst. & Gynec., 50: 691-700, 1945

As granulosa cell tumors have become more commonly recognized it is apparent that the prognosis is more difficult to determine than formerly believed. It was at first thought that these tumors were benign. As the number of case reports multiplied and follow-up studies were available, it became evident that the granulosa cell tumor, although more benign than most other ovarian carcinomas, nevertheless carries with it a definite malignancy. The difficulty in the prognosis of the granulosa cell tumor is further reflected by the wide variation of statements in the literature concerning its malignancy. The occurrence of malignancy among the granulosa cell tumors is quoted by various authors as being as low as 10 per cent and as high as 55 per cent, with all intermediate gradations.

The authors report three cases demonstrating that the prognosis in individual cases of granulosa cell tumors is most uncertain. In all three cases the tumors were considered benign at the original operation in spite of excessive fluid being present in the abdomen in two. They were well encapsulated and there was no evidence of metastases or implantation; in only one case was there a rupture of a small lobule with the escape of serous fluids—a circumstance which might possibly be considered a factor in disseminating the process. All three patients were apparently well and healthy over a period of at least fifteen years, and yet all died of the disease eighteen, twenty, and twenty-one years, respectively, after the original operation. One case recurred in spite of a bilateral salpingo-oophorectomy and a hysterectomy. Another case with wide-spread inoperable abdominal metastases responded well to deep x-ray therapy over a period of three years, but a subsequent recurrence of the growth proved refractory to treatment.

Total urinary estrogen values were not extremely high in two cases but within the range of values for normal cyclic women. However, the values were well above those usually found in this laboratory for postmenopausal women into which age group all three patients fell at the time of the recurrence. All three cases exhibited clinical signs of estrogenic activity on recurrence of the tumor.

(In spite of the fact that granulosa cell tumors have been well known to gynecological pathologists for a good many years, there is still a paucity of reports as to the ultimate outcome in large groups of cases, and the results in these show considerable discrepancy. The majority of papers dealing with this tumor type have to do with single cases, or very small groups, reported usually soon after observation because of the comparative rarity of these tumors or the biological effects which they often produce. The present report of the 3 instances of very late recurrence of granulosa cell tumors serves a useful purpose as illustrating the uncertainty of prognosis. Furthermore, most authors have found the histological characteristics of little prognostic value. Everyone is agreed that the degree of clinical malignancy is far less than that of the common solid or cystic forms of ovarian

carcinoma, but there is no justification for the attitude of some pathologists in considering them comparatively harmless.—Ed.)

## GRANULOSA CELL TUMOR OF THE OVARY. A CLINICAL AND PATHOLOGIC REVIEW OF SIXTY-TWO CASES

JANE E. HODGSON, MALCOLM B. DOCKERTY, AND ROBERT D. MUSSEY

Surg., Gynec. and Obstet., 81: 631-642, 1945

This paper gives a report on the 62 cases (1.63 per cent) of granulosa cell type tumors encountered in a series of 3,800 ovarian neoplasms at the Mayo Clinic between 1910 and 1944. The patients with this type of tumor ranged in age from 17 months to 72 years, the average age being 52 years. Fifty-four of the 62 patients were married and eight were single. Of the married patients, 12 were nulliparous, 27 were primiparas and 15 were multiparas; the total number of children was 108. Although it appears that parity of the women might have been an influence, parity appeared to have no influence on the development of a granulosa cell tumor. Three of the nulliparous patients became pregnant after the surgical removal of the tumor.

Uterine bleeding, the most common complaint, was present in 46 cases. In the one case in which the patient was of prepuberal age, periodic vaginal bleeding had occurred at the age of 17 months. Of the 23 patients who were considered to be in the reproductive period, 13 suffered from menometrorrhagia of varying duration. In ten of this latter group, the bleeding had been preceded by episodes of amenorrhea lasting from 1 to 7 years. Bleeding was present in all of the 38 patients who had passed the menopause. Amenorrhea was a complaint in 22 per cent of the cases and abdominal enlargement in 29 per cent. From a study of the records it was apparent that the tumors grew slowly and might have been present for as long as 35 years. Urinary assays performed in one case were positive for eight rat units of estrogen per liter of urine excreted during the first 24 hours after operation. The excretion of estrogen dropped to zero during the next 24 hours. Further evidence of hyperestrinism in this series of cases was afforded by symptoms of precocious puberty, amenorrhea, postmenopausal bleeding, and the incidence of adenomyosis and endometriosis (9.6 per cent), uterine fibromyomas (51.6 per cent), uterine hypertrophy (59.6 per cent) and proliferative endometrium (67 per cent). Endometrial carcinoma was observed in eight of the 38 postmenopausal patients. In three of these eight, carcinoma of the breast with axillary metastasis also developed. This phenomenon of coexistent ovarian, endometrial, and mammary carcinoma bears a striking similarity to the results of experiments on laboratory animals in which estrogen stimulation appears to be a factor in carcinogenesis.

Pathologically, the tumors appeared to be of a low order of malignancy, with 45 cases in Broder's group 1 and 17 cases in group 2. Follicular, cylindroid, diffuse and pseudoadenomatous cell patterns were all represented in the series.

Twelve of the tumors presented microscopic features of combined theca cell and granulosa cell elements.

Chemical analyses of four tumors indicated an excess of cholesterol esters as compared to the normal content of these substances in the ovaries. The phospholipid content of the tumors was surprisingly low. Analysis of luteinized portions revealed increased amounts of both substances.

In the total series of granulosa cell tumor there were four definite recurrences and one possible recurrence. Conservative procedures among postmenopausal patients accounted for four and possibly five failures to obtain good results. Four recurrences and three deaths occurred in this group. This incidence of recurrences among older patients indicated that bilateral oophorectomy with hysterectomy is advisable for tumors of this type affecting women past middle life. Less radical procedures are apparently indicated for granulosa cell tumor among younger women as no recurrences were noted in this group and pregnancy subsequently occurred in three cases.

## A GRANULOSA CELL TUMOUR OF TUBULAR OR ADENOMATOUS TYPE

DANIEL DOUGAL

J. Obst. & Gynaec. Brit. Emp., 52: 370-71, 1945

The author presents the case of a 22-year-old woman who consulted him with the complaint of continuous uterine hemorrhage of 17 months' duration with some backache. Previous medical and surgical history were negative. The menarche had occurred at the age of 11 years. The patient was well-developed and showed normal secondary sex characteristics. She was somewhat anemic as a result of the excessive bleeding. Abdominal examination was negative. Vaginal examination revealed a normal uterus, but in the position of the right ovary was a readily palpable solid tumor of about the size of a tennis ball.

Following a diagnosis of granulosa cell tumor, the patient was subjected to operation. In addition to the tumor there was found evidence of an antecedent pelvic infection in the form of light film-like adhesions about the uterus and appendages. The tumor involved the right ovary and had the corresponding Fallopian tube stretched over it. A right salpingo-oophorectomy was performed. The patient recovered and during the 3 years which have elapsed since operation has been perfectly well and has menstruated normally.

The specimen was a solid ovarian tumor, 3 inches in diameter, encapsulated, somewhat lobulated and of a bright yellow color. Macroscopic appearances conformed with the pre-operative diagnosis of granulosa cell tumor and it was expected that on microscopic examination this diagnosis would be confirmed by finding the usual folliculoid, cylindroid or sarcomatoid arrangement of the

granulosa cells composing the tumor. Actually, the tumor consisted of a mass of perfectly-formed tubules. The general arrangement of tumor and ovary suggested that the tumor had not originated in the ovarian cortex but in the medulla or hilum. The tumor was an encapsulated, luteinized and hormonally active adenoma of the ovary. 3 references.

## CEREBRAL METASTASES OF OVARIAN STRUMA

L. DE BAKAY, JR. AND F. DE LEHOCZKY

*Confinia Neur.*, no. 1, 22-31, 1944

The proportion of malignant tumors with cerebral metastasis has been estimated as from 10 per cent (Dandy) to 17 per cent (Gorland, Armitage and Grant). The following order of frequency by site of tumor has been established by brain surgeons: lung, breast, adrenal, stomach and intestines, and ovary. In this paper a case report is given of cerebral metastasis of the least frequent type, i.e., originating in the ovary. This case is believed to be unique in the literature because of the presence of thyroid tissue.

The patient was a 57-year-old woman who, a year prior to her death, began to complain of general weakness and staggering gait. These symptoms increased during the year and later hyperthyreosis and signs of a supratentorial disturbance developed. The general symptoms of brain tumor, such as headache and nausea, were missing, but forgetfulness and indifference developed in the last 2.5 months before death. At operation a tumor the size of a nut and resembling a struma, was removed from the anterior part of the right frontal parietal region. A study of the patient's history revealed no evidence that she had ever had a struma, nor could any alteration, enlargement or node be found in the thyroid. However, six or eight years previously a dermoid cyst of the ovary had been removed which histologically consisted of typical tissue. At the time she was operated upon for the ovarian tumor she had no symptoms pointing to hyperthyreosis and her basal metabolism was normal (+3.3). When her neurological symptoms appeared her basal metabolism had increased to +34. This increased metabolism is explained by the histological picture showing hyperfunction of the struma metastases arising in the skull bone and brain.

## THE PROGNOSIS OF DISGERMINOMA OVARIUM

RIEBEN (BASEL)

*Monatschr. f. Geburtsh. u. Gyn.*, 119: 161-164, 1945

Twenty-three cases of dysgerminoma of the ovary are reported; 15 were of more than 5-year duration. The paper is concerned primarily with prognosis

and sensitivity of the tumor to x-ray therapy. In most cases only one ovary was affected; about 50 per cent of the cases were in women aged 16 to 25 years, and in three cases the tumors complicated pregnancy. In one of these latter cases the tumor was first found sub partu as an obstruction to the birth process. This woman, as well as the two others, was delivered by cesarean section and the tumor removed at the same time. One of the women received no x-ray therapy. At her death 5 years later from pneumonia no recurrence was noted. Another received x-ray therapy postoperatively, but extensive metastases developed in the omentum and unirradiated portions of the epigastrium. A total cure was not effected in spite of radiation therapy. Sufficient time had not elapsed in the third case to permit definite conclusions on the outcome.

Two cases in which cures were effected by x-ray are reported in some detail. One was in a 17-year-old patient whose tumor had been only partially removed at operation. In the other metastases had developed in the lumbar vertebral column and progressed to paraplegia.

Of the 15 patients who had suffered from ovarian dysgerminoma for over five years, seven were living and free from recurrences at the time of the report. All four of those over 40 years of age died.

It is concluded that the prognosis can be improved if close watch is kept for metastases which, in the case of dysgerminomas can be very rapid, and by radiating at the time of treatment of the primary growth those glandular regions in the retroperitoneal area which are most likely to become affected. The sedimentation rate, which usually increases in metastases, may be used as an aid to diagnosis.

Data from the author's records and those of other hospitals in Switzerland give the percentage of 5-year cures of ovarian dysgerminomas as 46.6; for other malignant ovarian tumors this percentage is given as 29.1.

Editorial note on abstract of article by Rieben

(The spelling of this tumor designation has been changed in this abstract, as "dysgerminoma" appears to be establishing itself as the preferred form. It is the one used in such official indices as the Quaterly Cumulative Index.—Ed.)

## FOLLICULAR CYST SIMULATING CORPUS LUTEUM CYST

WASHINGTON BUNO

Rev. Asoc. Med. Argentina, 59: 784-787, 1945

A case report is presented of a 42-year-old woman who was operated upon for uterine retroversion and myoma, four days before an expected menstrual period. During the course of the operation an ovarian cyst, the size of a hazel-nut and containing clear liquid, was found. The surface of the cystic cavity was bright, very smooth and regular and gave the impression of epithelization. Typical luteinic tissue was found on almost the entire extent of the wall of the cyst, and an initial macroscopic diagnosis of a corpus luteum cyst was made. On further

examination, however, it was seen that a black, hemorrhagic arch of irregular thickness extended along the luteinic tissue. This hemorrhagic arch lay in the middle of the luteinic tissue and between it and the cystic cavity there was a fringe continuous with the tissue, the external borders of which were discretely wavy. The hemorrhagic arch stopped at a certain distance from the extremity of the luteinic wall and was encompassed at both ends by luteinic tissue. On histological examination, the wall of the cyst presented two luteinic fringes with paraluteinic glandules and between the fringes a hemorrhagic connective tissue. The histological diagnosis was a follicular cyst with a discontinuous epithelial reinforcement, almost completely surrounded by a flattened and deformed, but not cystic, corpus luteum.

### THE RUPTURE (INTRAPERITONEAL, INTRA-INTESTINAL AND INTRAVESICAL) OF SUPPURATIVE PELVIC MASSES, WITH AN ANALYSIS OF 53 CASES FROM CHARITY HOSPITAL OF LOUISIANA AT NEW ORLEANS

HILLIARD EVE MILLER

New Orleans M. & S. J., 98: 115-122, 1945

In the literature spontaneous ruptures of pelvic inflammatory masses are usually reported singly or in small groups, from which it is generally assumed that such accidents are rare. From analyses of records of the Charity Hospital of Louisiana, which are reported upon in this paper, the author draws the conclusion that while such ruptures are more uncommon than suppurative pelvic processes they are an important cause of death in pelvic inflammations.

The records of the hospital over a 17-year period revealed 44 cases in which pelvic masses had ruptured spontaneously into the peritoneal cavity, 6 into the intestinal tract and 3 into the urinary tract. During a 6-year period there were an additional 97 cases in which inflammatory pelvic masses had accidentally ruptured into the peritoneal cavity in the course of operation.

In 3 of the cases of spontaneous rupture, the onset of symptoms began immediately after a fall or other accident; in 3 cases onset of symptoms followed closely upon pelvic examination. In 6 cases the patients took purgatives following the onset of pelvic pain but whether purgation precipitated rupture or merely aggravated it was not recorded. Twenty-one of the patients had had recent infections lasting from a few days to four weeks; the same number had had recurrent acute attacks and many were being cooled in preparation for surgery. Clinically the cases fell into two groups. One group presented all the symptoms and signs of an acute abdominal catastrophe, including violent pain, vomiting, tenderness and rigidity, usually associated with shock. In the other group the symptoms and signs were chiefly those of acute pelvic inflammation, including pain, nausea

and vomiting, menstrual and urinary tenderness, diarrhea, chills and fever, tenderness, rigidity and distention. In only the extremely acute cases was it possible to determine the exact moment at which rupture occurred. Usually it was impossible to determine which symptoms were due to the basic pelvic disease and which to the superimposed accident. In only 2 of the cases had rupture been considered a possible diagnosis.

Thirteen of the patients were in the hospital when the accident occurred. All of these died, except one who was operated upon immediately after the mass had been ruptured during a bimanual examination. The only other patient in this group who was operated upon died four hours after the operation and nine hours after the rupture. In the total group 12 were operated upon. Simple drainage was carried out in 8 cases, with 6 deaths; salpingo-oophorectomy in 2 cases, with 1 death; removal of the adnexa combined with supravaginal hysterectomy in 1 case, which was fatal; and in 1 the exact pathologic process remained unrecognized until necropsy. Powdered sulfanilamide was instilled into the peritoneal cavity in 3 of the surgical cases, with survival in one instance. Parenteral chemotherapy was used in 2 other surgical cases, with survival in both instances. These 3 represented the only survivors in the entire group. No patient for whom the exact time of rupture could be determined lived longer than 48 hours without operation.

Of the 97 patients whose pelvic masses were accidentally ruptured at operation, 6 died (4 of peritonitis, 1 of shock on the operating table, and 1 probably of embolism). Possible explanations for the less catastrophic consequences of rupture in this group are considered as follows: (1) many of the patients had been thoroughly cooled before operation and the pus can be assumed to have been sterile; (2) the general peritoneal cavity was usually well packed off when the rupture occurred; (3) the accident was recognized at once, and the spilled pus was promptly removed by suction and other methods; (4) intraperitoneal chemotherapy was used in most of the cases. Chemotherapy had not been employed in 5 of the 6 cases with fatal outcome.

(This must have been about the last paper written by the late lamented Hilliard Miller, one of the leading gynecologists of the South. Only a very large clinic, like the Charity Hospital in New Orleans, with its great numbers of complicated pelvic inflammatory cases, could have yielded such a large group in which this relatively rare complication had occurred. To those of us who have seen only a very occasional case, the high mortality rate will seem surprising. For example, of 13 patients in whom the accident happened after admission to the hospital, 12 died. Most of the cases apparently occurred in the acute stages of pelvic infection, in which case, as Miller states, it is difficult to determine whether the symptoms are due to the pelvic infection itself or to the superimposed accident. Since the series covered 17 years, sulfa therapy was available to only a fraction of the cases. While the group has not been sharply subdivided on this basis, it would seem, from the mention of several instances in which it was used, that it must have been of great value. A bacteriological report on the cases in this large series would have been of great interest.—Ed.)

## FEMALE UROLOGY

### URINARY STRESS INCONTINENCE IN THE FEMALE. A COMBINED GYNO-UROLOGICAL APPROACH TO ITS CORRECTION

WALTER J. REICH, J. LESTER WILKEY, AND HAROLD E. SILVERMAN

Amer. Jour. Surg., 70: 341-353, 1945

In view of the fact that there is an average recurrence of about 20 per cent of the cases of incontinence after attempts at its surgical correction, the authors stress the importance of a more carefully combined gynecological and urological study of the causative factors, after the exclusion of systemic disturbances, plus a meticulous anatomic restoration of the damaged tissues. This gynecological study should be preceded by detailed history taking, a complete physical examination to determine the status of all systems, complete laboratory procedures and an x-ray of the lower spine. The x-ray may sometimes reveal an often unsuspected occult spina bifida which is a very frequently overlooked cause of urinary incontinence. Cystourethroscopy has been found a valuable means of discovering etiologies of incontinence which are not due to pure anatomic changes and which, herefore, can not be corrected by surgical repair. Some of these occasionally overlooked "non-operative" causes of incontinence are chronic follicular urethritis and trigonitis, paradoxical incontinence, bladder diverticulas, with a concomitant low grade inflammatory process, urethral diverticulas, suburethral cysts, ball-valve polyps or stones, and strictures of the urethra. In addition to childbearing, which is the usual etiology of the so-called "true operative cases," other causes such as coitus against congenitally weak tissues, trauma, continued friction from horse-back or bicycle riding, and chronic masturbation of the intravaginal type should be taken into consideration. Normally the long axis of the urethra is at right angles to the floor of the bladder. In the "true operative cases" this angle is decreased, and in the severe cases there is no angle whatsoever present.

Although the internal urethral sphincter plays a very important role in the continence of urine, its repair alone, as is sometimes attempted, is not sufficient in the correction of impaired urinary control. The so-called uteropubic fascia or pubocervical muscle is a loose and condensed connective tissue which is associated with the angle between the base of the bladder, the urogenital diaphragm, and the medial margin of the levator ani on either side of the midline, uniting the bladder to these structures, and the structures to one another. The downward prolongations of this pubercervical tissue also extend between the bladder base and anterior vaginal wall. Here it is of a loose areolar type and a line of cleavage is easily found and followed in the process of separating the anterior vaginal wall from the bladder base during cystocele repair. When the dissection is at an end,

the pubocervical tissue is found on the presenting surface of the vesical fundus. By properly plicating the tissue a portion of the platform upon which the bladder rests is made taut, and the fundus vesicae therefore elevated on its transverse longitudinal axis. By thus doing away with the abnormal pouch of the bladder, the drag is taken away from the posterior urethral wall, especially in the region of the internal voluntary and involuntary sphincters, and aids in restoring urinary continence. Between the posterior urethral wall and the anterior vagina, the urethral tube is exceedingly firmly adherent and imbedded, so that the muscularis of the urethra and the muscular coat of the vagina are in firm contact with one another. Therefore, no plane of cleavage exists between these two organs and to expose the urethra its muscular coat must be directly separated from the muscularis of the anterior vaginal wall in order to avoid serious injury.

A properly executed operation for the cure of urinary incontinence should include the plication of the peri-urethral levator fibers in order to angulate or tighten the tube postero-anteriorly. A subvaginal approximation of the attenuated pubococcyge and their overlying fascia serve to take up the slack in the pelvic floor, thereby raising and strengthening the foundation which supports the vesical fundus and first part of the urethra. Since the urethral levator sphincter is derived from the pubococcygei, this sphincter must be further tightened. The peri-urethral fibers of the sphincter urethrae muscle should be plicated and the posterior border of the urogenital diaphragm should be identified if possible, and made taut by reefing or plication. This latter maneuver aids in the firmer anchorage of the urethra, as well as in the reinforcement of the genital hiatus. The stretched or lacerated bulbocavernosus fibers which are found peri-urethrally should be sutured. In addition the retracted posterior ends of the bulbocavernosus muscle should be restored by suture during performance of the perineorrhaphy.

The *modus operandi* of labor in the production of incontinence is described.

A description, with illustrations, is given of a suggested new operative technique. Preoperative management includes the culture of urine and, if virulent organisms are found, treatment is continued until the urine is definitely clean, before operation is attempted. In addition to the usual postoperative treatment, daily or twice daily bladder irrigations through the Foley bag are carried out. Potassium permanganate 1:10,000 solution is employed, and in cases in which alkaline infections were found, irrigations with sterile citric acid titrated to a pH of 4 are used. Mandelic acid or sulfonamides are sometimes given by mouth. The Foley bag is left in situ for seven or eight days. About three weeks after the operation the urethra is dilated with ordinary Hegar urethral dilators in order to alleviate bladder spasms and to stretch the scar tissue formed about the urethra.

## DIVERTICULUM OF THE FEMALE URETHRA; REVIEW OF LITERATURE WITH CASE REPORT

IRA G. DOWNER AND FRANK D. VIRGILIO

*J. Urol.*, 54: 53-58, 1945

Literature with reference to definition, incidence, etiology, symptoms, and treatment of diverticulum of the female urethra is reviewed. The following conclusions are drawn. Although cases believed to have been of congenital origin have been reported, the vast majority of cases are acquired, either from inflammatory processes or trauma. Exact statistics as to the frequency of this lesion are not available, but it is believed to be more common than reported. Diagnosis is, as a rule, not difficult if the condition is borne in mind, and may be made absolute by urethroscopy and urethrography. Excision of the sac is the treatment of choice and results in prompt relief of symptoms.

A recent case seen by the authors is reported. The patient, aged 36 years, complained of a tumor of the vagina and dribbling of urine following the emptying of the bladder. She had been aware of the mass for 15 years, but did not seek medical aid until coitus became very painful and the size of the mass and leakage of urine became very annoying. Her past history was irrelevant except for an inflammation of the vagina and pelvis two years prior to her notice of the mass, and her only pregnancy had terminated in a 3-month abortion. On digital pressure the mass felt cystic and turbid urine exuded from the external meatus. Cystoscopic examination revealed a diverticulum located between the bladder, urethra and vagina, and roughly one-third of the way from the internal sphincter to the end of the urethra. Under nitrous oxide and oxygen anesthesia the patient was placed in lithotomy position and the sac was dissected down to the neck and excised. The opening into the urethra was closed over with interrupted chromic sutures, the vaginal layers were approximated with interrupted chromic catgut, and the vagina was packed with gauze. The gauze was removed on the fourth day and the indwelling catheter was taken out on the tenth day. The wound healed completely in 11 days and, when last seen about 2.5 months after operation, the patient was completely cured. Microscopic sections revealed the mucous membrane covered by transitional stratified epithelium, which for the most part was desquamated. A diagnosis of diverticulum of the urethra with pyogenic infection and ulceration was made.

## THE RECURRENCE RATE OF URETHRAL CARUNCLES

PERCY MALPAS

*J. Obst. & Gynaec. Brit. Emp.*, 52: 367-369, 1945

A series of 85 cases of urethral caruncle were treated by the author over a period of 15 years. The caruncle recurred in 27 of 68 of these cases which were

treated by excision. The greatest number of recurrences occurred within 5 years of the treatment, mainly in the 2nd, 3rd and 4th years. The presence and treatment of an associated lesion such as an infection or a prolapse did not seem to have any bearing on the chances of recurrence.

Fifteen cases were treated by coagulation diathermy and recurrence was not seen in any of these. An electro-cautery was used after excision in 6 cases with results indicating that the effect of a cautery is not deep enough to prove adequate. Radium was used experimentally in 3 cases. The author found that the radio-sensitivity of a urethral caruncle is no greater than that of the normal urethral mucosa and, as a primary method of treatment, radium is not advisable, though it has a limited scope in the treatment of recurrent caruncle.

General clinical experience would seem to discount the possibility of malignant change as a cause of recurrent caruncle.

(Recurrence of urethral caruncles can occur after any of the methods of removal mentioned by the author. Whether coagulation, simple excision, or excision followed by the electro-cautery is to be employed will generally be decided, not only by the personal preference and experience of the operator, but by the individual circumstances of the case, especially as regards the size and site of the caruncle.—Ed.)

## THE OPERATIVE TECHNIQUE OF COMPLICATED VESICO-VAGINAL AND URETHROVESICOVAGINAL FISTULAS

S. N. HAYES

Surg., Gynec. & Obst., 81: 346-354, 1945

The author describes an operative technique for complicated vesicovaginal and urethrovaginal fistulas, summarizing 16 years of experience. Pre-operative and postoperative care is considered. Of the 85 patients in the group presented, 73 were cured. Only 8 cases were simple. Two patients died, one of uremia on the 4th day, the other of blackwater fever. In 5 cases, rectovaginal fistulas were present and were operated on prior to the vesicovaginal fistula. In two cases the urethra was entirely absent. A percentage cure rate of 89.85 per cent, considering the variety and complications encountered, is adequate proof that the flap splitting operation is a satisfactory operative method.

Three types of complicated fistula are illustrated: (1) lateral type, adherent to the descending ramus of the pubis; (2) type with the upper portion of the urethra involved and which requires reconstruction; and (3) large fistulas. A careful preliminary study of the fistula is essential. Complicated fistulas may be accompanied by stenosis of the vagina in all degrees, fibrous bands (most commonly a transverse band at the lower border of the upper third of the vagina, causing an hour glass contraction) and impairment of the mobility of the cervix. Size, shape and position of the fistula may further complicate a case. Finally, the urethra may be partially or, rarely, entirely destroyed.

The large majority of fistulas can be cured by one operation. Of the 85 operations in this series, 78 were one stage. Large fistulas may require a two

stage operation based on reducing the size of the fistula. Incidentally, the size of the fistula is no criterion of its curability. Preoperative treatment includes relieving cystitis by bladder irrigation, sitz baths for excoriations of the vulva and thighs followed by an ointment of zinc oxide and lanolin. Tincture of iodine or other antiseptic is used to paint the operative field in preference to drugs said to be urinary antiseptics.

The patient is placed in the lithotomy position with the buttocks elevated so as to provide the best possible exposure. The labia minora are sutured to the inner portions of the thighs. For complicated cases, Schuchardt's incision, made on the left or right side, will provide the necessary additional exposure. Hemorrhage is usually considerable during operation. Infiltration of the operative area with adrenalin reduces the amount of oozing. Hemostasis by means of forceps and ligature is not attempted. Any visible bleeding point is controlled by underpinning with needle and catgut. The author describes the steps of operation including exposure of the fistula or urethra or both, procurement of mobilization with special reference to cases where the urethra is destroyed, and suturing. The vagina is tightly packed with gauze for 8 hours.

Postoperative treatment is based upon two principles, namely, (1) to keep the bladder empty, and (2) to keep the stitches clean. An indwelling catheter is used for at least 21 days. The stitch line is regularly syringed with normal saline administered with a 10 cc. syringe and intramuscular needle.

In the event of failure on first operation, the second operation should not be performed for at least six months. Fistulas resulting from an attempt at repair contract to a remarkable degree and no object is gained by a second early operation. Pin point fistulas resulting from an operation invariably heal spontaneously. 6 references. 9 figures.

(In the preceding issue of the Survey (February), there were abstracts of two excellent papers from clinics in India dealing with this same subject, one by Thomas and one by Thompson (pp. 136 and 137 of February number). The paper by Hayes again emanates from India, and like the two mentioned above, it presents a masterly review of a large series of cases, with an excellent discussion of the principles and technique of the operative treatment employed, especially in the obviously difficult group which made up a considerable proportion of the total series. That 73 of a total of 85 patients of this series were cured speaks well for the methods employed, especially since only 8 of the 85 were of the simple variety.

The description of some of the complicated cases, some very large, some fixed to the rami, some associated with destruction of the urethra, and some complicated by fixation and cicatricial stenosis of the vagina, makes it abundantly clear that the group was anything but "hand-picked." The fact that 78 of the 85 operations done were of the one-stage variety, and that the great majority of the fistulas were cured by a single operation, is eloquent testimony to the soundness of the operative techniques employed.

The emphasis which the author puts on such accepted principles as free mobilization, the frequent employment of the Schuchardt incision, and meticulous pre- and postoperative care, no doubt explains his good results. From the large series of cases being reported from India one may conclude that urinary fistulas are much more common in that country than here, and it may be fair to conclude that this is to be explained by the poor type of obstetrical care available there. In our own country an increasing proportion of urinary fistulas is the result of surgical operation, with still not a few the result of radium therapy for cancer, or of the latter disease itself.—Ed.)

## OPERATIVE GYNECOLOGY

### COMPLETE ABDOMINAL HYSTERECTOMY: IMPRESSIONS BASED ON 135 CASES

ROY W. MOHLER AND EDWARD H. BISHOP

Am. J. Obst. & Gynec., 50: 489-495, 1945

This paper discusses the merits of complete abdominal hysterectomy based on an experience of 135 operations done with a similar technique and by the same personnel. There was no mortality in this series and, in the authors' opinions, the mortality of the operation should not be greater than that of other gynecological procedures; nor should the immediate temperature morbidity be higher.

After presenting their operative technique in detail, the authors give especial consideration to granulations in the vault of the vagina, support of the vaginal vault, shortening of the vagina and development of normal vaginal biology.

Granulations in the vault of the vagina occurred in 27 per cent of their patients. These areas have never been extensive and have usually occurred at the lateral angles of the vaginal incision. They have been managed by curetting the granulation tissue a few weeks following operation. If these areas are not destroyed they will produce an abnormal vaginal flora and consequently a leucorrheal discharge. Meticulous closure of the vault helps in their prevention.

The support of the vaginal vault is not dependent upon the presence of the cervix. Prolapse of the vault of the vagina has not occurred in this series and the authors believe that it should not occur provided proper attention is given to the fixation of the paravaginal fascia, the round ligaments, the ovarian pedicles and the uterosacral ligaments to the vaginal vault.

Vaginal shortening because of removal of the cervix was observed but once and in some instances it was the authors' impression that the vagina was lengthened. They do not believe that removal of the cervix without vaginal repair could alter the length of the vagina sufficiently to interfere with complete or satisfactory coitus.

It is the authors' opinion that normal vaginal biology exists after complete hysterectomy and that the climacteric occurs at its normally expected time when the ovaries have been conserved.

(The technique employed by the authors is about that used by most operators, making allowance for the usually unimportant tricks and touches added by each individual. They describe it in meticulous detail, very properly stressing the importance of preoperative preparation of the vagina. They do not drain the vaginal vault, in which practice most gynecologists will agree with them, except for specific indications. While postoperative granulations in the vaginal vault occurred in 27 per cent of their 135 cases, this rather high figure may have been due to the thoroughness of the follow-up, without which they are often overlooked. As the authors say, such granulations can be readily taken care of by the

curette, or perhaps better in my experience, by the electrocautery. The bugbear of vaginal shortening, so often brought forward against total hysterectomy, finds no support in the experience of the authors, and this has been my own observation. The occasional occurrence of dyspareunia is better explainable, it seems to me, by the tenderness of the vaginal scar in some cases rather than by any shortening of the vagina. As I have mentioned in a previous comment, the long drawn out controversy over total vs. subtotal hysterectomy appears to be drawing to a close, although every one should appreciate that there is a place for both. However, the total technique is clearly preferable unless there is some contraindication imposed by the individual circumstances of the case or by the surgical limitations of the operator.—Ed.)

## VAGINOPERITONEAL FISTULA WITH CHRONIC PERITONITIS FOLLOWING VAGINAL HYSTERECTOMY

E. W. BERTNER AND K. C. VON POHLE

Texas State J. Med., 41: 264-266, 1945

A case report which appears to be unique in the literature is presented. It deals with a Negress whose chief complaint at admission to hospital was weight in the pelvis of 4 or 5 years' duration. On vaginal examination a diagnosis of cystocele, urethrocele, rectocele and fibromyomata uteri was made. Vaginal hysterectomy, with anterior and posterior repair, was not unduly difficult and the postoperative course was as expected the first two days. On the third day the patient became febrile and had marked tenderness in the left costovertebral angle and about ten days later began to have profuse vaginal discharge. Sulfathiazole was given without effect. An opening of a sinus tract high in the vaginal vault could be visualized at bimanual examination, and about a month later was seen roentgenographically. During this time she had no complaints other than the foul vaginal discharge and temperature. At exploratory laparotomy the peritoneum was found to be markedly injected and thickened, the bowels were densely adherent to each other and showed the typical results of a massive peritonitis. The subdiaphragmatic area and the perirenal areas were free of any pathological conditions. There was no collection of pus in the pelvis nor were any foreign bodies found. Drains were placed into the pelvis and into the general abdominal cavity, and the abdomen closed in layers. Cultures taken from the abdominal cavity were reported negative for bacteria. Examination of the biopsy specimen of the peritoneum revealed only a chronic peritonitis with calcium deposit. The patient's course continued the same as previously. General supportive measures included transfusions and vitamin therapy. As soon as penicillin became available, the patient was given 100,000 units intramuscularly daily for five days. Her temperature became normal in six days from start of the penicillin therapy. She was discharged from the hospital a week later. Within four months the sinus had completely closed and there was no vaginal discharge.

(This case, on the basis of the data embraced in the above abstract, would appear to represent a lower abdominal peritonitis, with persistence, not surprising under such circumstances, of a discharging sinus through the vaginal vault. I would doubt that the case can be considered "unique in the literature." Minor degrees of such infection, more often extraperitoneal rather than peritoneal, have probably been observed from time to time by those doing any great number of vaginal hysterectomies.—Ed.)

## PREPARATION OF THE DIABETIC PATIENT FOR OPERATION

GEORGE GRAHAM

Proc. Roy. Soc. Med., 38: 547-549, 1945

The author states that nowadays diabetes is in no wise a contraindication for any operation provided that (1) a physician is at hand who knows how to look after these patients; (2) adequate facilities are available for estimation of the blood sugar; (3) the best anesthetic is chosen and given by a good anesthetist; and (4) the operation is well and quickly done.

The anesthetic is very important and a local or spinal anesthetic causes the least disturbance. Gas and oxygen is the next best, provided sufficient oxygen is given to prevent any cyanosis. Intravenous pentothal and evipan produce no ill effects. If ether is necessary to obtain complete relaxation, it should be given in small amounts. Avertin is better not used and chloroform should never be used because of its action on the liver.

The diabetic condition of the patient should be as well controlled as possible prior to operation. If the diabetic condition is mild and the patient taking no insulin, but having a small amount of carbohydrate, it is well to correct the low glycogen content by increasing the carbohydrate intake to at least 150 grams and giving a small dose of insulin for two or three days before the operation. If the patient is having insulin but is passing a good deal of sugar it is well to increase the insulin for a few days and thus stabilize the condition. In choosing the type of insulin, the author considers it best to use the ordinary or quick-acting insulin since slow-acting insulins do not act quickly enough to control the rise in blood sugar caused by the anesthetic and are more likely to allow hypoglycemia.

On the day of operation, morphine is always given to quiet the patient in as small a dose as possible, perhaps  $\frac{1}{4}$ th grain of morphia. The patient should not be starved before operation but should be given his regular meals with glucose to ensure his having plenty of glucose in the liver and muscles and sufficient insulin as indicated. If the operation is scheduled at a time well after any meal, the patient should be given an additional dose of insulin and glucose about two hours prior to the operation. If the patient does not regain consciousness from the anesthetic in a satisfactory manner, an intravenous injection of glucose is effective in some cases.

In the case of emergency operations, should the patient be passing much sugar and some acetone bodies, the supplementary insulin for the anesthetic should be increased. If he is very ill much larger doses both of insulin and of sugar should be given. Large doses of insulin will be needed after operation if coma is to be prevented and the blood sugar should be estimated at frequent intervals.

(As the author states, diabetes no longer constitutes a very serious hazard in surgical operation, provided that the patient is subjected to proper preliminary study and management, as well as postoperative surveillance. In such cases the gynecologist will always wish to have the help of an internist trained in the management of diabetes.—Ed.)

## STERILITY

### THERAPEUTIC ASPECTS OF UTEROTUBAL INSUFFLATION IN STERILITY

I. C. RUBIN

Am. J. Obst. & Gynec., 50: 621-640, 1945

In the present paper the author endeavors to estimate the therapeutic value of uterotubal insufflation in sterility. For the majority of successful cases the therapeutic action appears to be the following:

1. *Establishing Patency of the Genital Tract.* Insufflation establishes patency of the genital tract from the external os of the cervix to the abdominal opening of the fallopian tubes. In addition, the introduction of the cervical cannula stretches the cervical canal somewhat, rendering it more patent for a varying period of time.

2. *Removal of the Cervical Plug.* In some cases a mucous plug, not visible at the external os but occupying the deeper portion of the cervical canal, is expelled after the cannula has been removed. The author has the impression that the dislodgment of the mucous plug may be an important factor in some cases.

3. *Effect on the Tubes.* Insufflation probably exerts its most valuable therapeutic action on the tubes. Its manifold action consists in separating mild agglutinations of the folds of the tubal mucosa, straightening out tortuous tubes, especially of the infantile type, dislodging a mucous inspissation from a narrow to a wider portion of the tube, and actually separating adhesions at the fimbriated end.

4. *Possible Psychic Effect.* Although the exact mechanism involved here is not clear, it may be that insufflation overcomes uterotubal spasm.

5. *The Therapeutic Effect of Repeated Tests.* In one instance the author has done as many as 18 tests on 1 patient. Altogether, the fallopian tubes of 438 of his patients showed improvement in patency on a second or third insufflation.

In the author's series of 3200 insufflations, 590 pregnancies occurred, that is in 18.4 per cent. About two-thirds of his patients represented cases of primary sterility and in those 2014 women, 358 pregnancies ensued, an incidence of 17.7 per cent. In the 1186 cases of secondary sterility the results were about the same, that is, 232 pregnancies, or 19.6 per cent. Realizing that some of these pregnancies might have occurred in the absence of insufflation, the author adduces evidence to show that after the third year of sterility, three times as many of his insufflated patients became pregnant as might be expected according to natural incidence. After longer periods of sterility his figures are even more convincing in showing that it was the insufflation and not chance which made pregnancy possible. In 38.6 of his patients the pregnancy occurred within two months after insufflation.

The author regards the kymograph as invaluable in these cases. He has used it in connection with tubal insufflation since 1925 and finds that it affords appreciable aid, especially in connection with prognosis and therapy.

(It is very fitting that this paper is included in the 25th anniversary number of the American Journal of Obstetrics and Gynecology, because it is just 25 years that Rubin presented us with the now universally employed method of tubal insufflation which bears his name. It is scarcely necessary to emphasize the fundamental importance or the very great value of this diagnostic method in the study of sterility. While other methods of tubal patency study have arisen, it is safe to say that the Rubin method is still the most popular of all.

The present paper, devoted chiefly to the therapeutic effects which the insufflation undoubtedly has in a proportion of cases, describes the probable mechanisms in such instances, and the illustrative cases cited by the author would appear in general to support his explanation. Moreover, he is conservative enough to suggest certain criteria which must be met in assuming that the insufflation does really, in the individual case, appear to have played a decisive role. The author's own rich experience is reviewed statistically and the paper also includes references to the experiences of others who have been impressed with the not infrequent therapeutic value of the method. I for one do not hesitate to tell patients that while the purpose of the test is primarily diagnostic, there is good reason to believe that it is also of real therapeutic value in some cases.—Ed.)

## AN INTERPRETATION AND EVALUATION OF TUBAL PATENCY TESTS

NORMAN F. MILLER

J. A. M. A., 129: 243-246, 1945

Uterotubal insufflation with carbon dioxide gas and uterosalpingography are today the two principal methods of studying tubal patency and physiology in the human. These tests should supplement each other for comprehensive evaluation of the part played by the tubes in the sterility of the female. When properly performed with full knowledge of both indications and contraindications, they are safe and highly informative. According to reports, approximately 60 per cent of women so studied present unequivocal evidence of tubal patency. About 30 per cent are found to have closed tubes.

The most important contraindication to the performance of a tubal patency test is the presence of genital tract infection. Pregnancy is an obvious contraindication and its nonexistence should be assured prior to tube testing. When uterotubal insufflation is contemplated, air should not be used because of danger of death from air embolism. The preferable time for determination of tubal patency is the week after menstruation. General constitutional disease and/or pelvic neoplasms associated with abnormal bleeding are other contraindications.

Whatever technique is used, determination of tubal patency depends on evaluation of the following points: (1) behavior of manometric pressure; (2) careful evaluation of subjective symptoms such as pain in lower quadrants; (3)

auscultation (of the tubes) over the lower abdomen; (4) checking for presence of shoulder pain following introduction of approximately 300 cc. of gas (patient sitting up); (5) noting the kymographic recording of intratubal pressure and activity; and (6) when uterosalpingography is used, the fluoroscopic observance of spill from the tubal ostiums. When these criteria are present it is safe to assume that at least one of the tubes is open. When they are absent, it is presumed that the tubes are closed. In general, tubal insufflation is the procedure of choice for initial investigation of patency. When stenosis or complete closure has been diagnosed, a further check by means of uterosalpingography may be desirable, since it permits more accurate localization of the obstruction and allows better selection of cases for salpingostomy.

In uterosalpingography, as with gas insufflation, excessive pressure must be avoided. For most informative and safe results, all oil injections should be carried out under fluoroscopic control. The opaque medium used should meet certain requirements: (1) give good contrast on roentgen visualization; (2) have sufficient consistency to permit ample time for study; (3) be neither too rapidly nor too slowly absorbed; (4) not cause irritation of mucous membranes or peritoneum; and (5) be safe to use. Lipiodol proves quite satisfactory although it has the disadvantages of slow absorption and possible irritant qualities. The presence of oil in the peritoneal cavity is proof of tubal patency.

On the basis of available data, it appears that less than one patient in a thousand suffers any morbidity following uterotubal insufflation. The author has been unable to find any recorded fatality following the use of carbon dioxide. Morbidity following uterosalpingography is higher. At least nine deaths have been reported following this test. Most trouble appears to have resulted from failure to rule out genital tract infection. Most fatalities following the use of either air or oil occurred in the earlier years when patency tests were in their developmental stage.

Uterotubal insufflation and uterosalpingography are both useful and should

be regarded as complementary procedures rather than as competitive tests. The author considers uterosalpingography an essential preliminary to contemplated salpingostomy. Both tests have a therapeutic as well as a diagnostic value. Doubtless success is accomplished by mechanical means through the removal of a mucous plug or old blood or the disruption of adhesions which may have been sufficient to interfere with the migration of the ovum. 18 references.

(Miller presents a sound and well-tempered evaluation of the two methods of tubal patency study which have established themselves as of undoubted value. Gynecologists are divided into two camps in so far as preference for one or the other method is concerned, but they should be friendly camps, because both methods are reliable, and perhaps ideally should be considered mutually supplementary. For routine everyday use the gynecologist is quite sure to accent one or the other in preponderant fashion. I have visited clinics in which oil injection is a part of the routine study of all cases of sterility. On the other hand, in my own community I believe this is only rarely employed, the carbon dioxide insufflation being overwhelmingly the routine method of choice, as it is in my own practice.

As a matter of "purely personal piffle," as O. O. McIntyre used to say, I like it because of its simplicity, its safety, its inexpensiveness to the patient, and its reliability when properly interpreted. It is not infallible, nor is the other method. For example, many of us have had the occasional experience of finding that reverse abdominal insufflation of supposedly closed tubes, on the basis of even repeated preoperative insufflation, has revealed them to be patent from above downward. But I know of similar experiences following oil injection.

The hazard of the Rubin method, when employed with such safeguards as Miller has mentioned, seems to me definitely less than that of oil injection. Apparently no fatalities have occurred when carbon dioxide is employed, as it always should be, while Miller has found that at least nine fatalities have occurred after oil injection. Moreover, there is risk, especially when undue pressure is employed, of the entrance of oil into the utero-ovarian venous system (intravasation) with pulmonary embolism in at least some of these cases. The most recent report on this subject is that of Roblee and Moore (South. M. J. 38: 89-94, 1945), who refer to 35 such cases in the literature, though there is some difference of opinion as to the harmfulness of such intravasation of the oil globules.

The one clear advantage of the oil injection method, and in my opinion the only one, is that it gives information as to the location of tubal closure, but gynecologists will be divided as to the practical value of this additional information in the majority of cases. Wherever the tubes may be blocked, the results of plastic restoration are so unsatisfactory that operations should never be urged upon the patient, and they are not justified unless the patient understands fully the relative slimness of her chances for later pregnancy. In any event the technique must be based on what is actually found by inspection and reverse insufflation rather than on any preoperative impression, and surprises in this respect are not uncommon. Of the operative procedures employed (salpingostomy, uterotubal anastomosis, and various types of cornual implantation of the ovaries) it is true that salpingostomy yields the least unfavorable results, though even when this alone is indicated, there is little room for enthusiasm. However, as Miller says, hysterosalpingography does here have its value in the selection of cases.

It is quite clear, I am sure, that I am prejudiced in favor of the Rubin method for routine use, but I have not the slightest criticism of the many fine clinicians who consider the oil injection method to be definitely superior. I suppose it is largely a matter of what method one has gotten accustomed to, just as one is apt to stick to one of the innumerable techniques of taking out an appendix, or just as one adopts direct cystoscopy in women as his favorite method rather than the indirect method, or vice versa. Whichever method of tubal patency study the gynecologist routinely employs, he should certainly appreciate the supplementary value of the other, and he should be familiar with the techniques of both methods.—Ed.)

## FEMALE STERILITY STUDIES

W. A. BEACHAM

Mississippi Doctor, 23: 424-427, 1945

The number of persons seeking information regarding sterility has increased appreciably in recent years and fortunately much progress has been made in the past decade in the study of sterility cases.

In conducting sterility studies, determination of the status of the male should precede a detailed investigation of the female. The reproductive organs should be thoroughly examined, prostatic and seminal vesicular secretions must be

studied grossly and microscopically and a specimen of semen should be examined. A complete "blood picture" and basal metabolic rate are indicated.

In the case of the wife, a complete history must be obtained and a thorough physical examination performed. One must obtain the pH of vaginal and cervical secretions which must be studied as wet and stained preparations. Vagino-abdominal and recto-vagino-abdominal operations must be accurately performed. A complete "blood picture" should be obtained and, when indicated, a basal metabolic rate determination and special blood studies should be made.

In ascertaining the occurrence of ovulation, basal rectal temperature charts should be kept but should not be substituted for microscopic study of the endometrium.

The author recommends hysterosalpingography as the best method of testing tubal patency. He suggests the following advantages of hysterosalpingography over salpingal insufflation: (1) a record is made in black and white of the status quo; (2) the site or sites of obstruction are accurately localized; (3) the internal configuration of the uterus is determined; (4) the position of the uterus is shown; and (5) size, contour, length and position of the unoccluded lumina of the salpinges are demonstrated. 6 figures.

(In some cases all of the procedures outlined for the study of sterility may be indicated, and at times still others. On the other hand, the ostensible explanation of the sterility may be revealed almost at the outset of the study, whether by the pelvic examination, the tubal patency test, or the semen examination. There would be no point to the continuance of very comprehensive study of the wife if the husband has a complete azoospermia. In other words there would seem to be no practical advantage to the couple in carrying out relentlessly and inflexibly the routine comprehensive programs advocated by some. While there are of course exceptions, the sensible and practical plan for the average gynecologist is often the step-by-step method, rather than to "shoot the works" with all possible methods of study when the couple present themselves. Beacham prefers hysterosalpingography to tubal insufflation for the routine study of tubal patency. Many others consider insufflation safer, simpler and just as accurate. This question was commented upon rather fully in the February issue of the Survey, p. 151.—Ed.)

## ASSESSMENT OF MALE FERTILITY BY SEMEN ANALYSES: AN ATTEMPT TO STANDARDIZE METHODS

CLARE HARVEY AND MARGARET HADLEY JACKSON

Lancet, 249: 99-104; 134-137, 1945

Methods employed at the Exeter Clinic of the Family Planning Association in the collection and examination of semen are described. For best results, the collecting tube should be of glass and warmed to blood heat, since cold glass seriously impairs the activity and reduces the viability of the sperm. Initial cooling should always be slow. Reliable conclusions about initial activity and viability can be drawn from specimens three hours old, but those obtained from older specimens are not so accurate.

A method is described of fixing and staining films of seminal fluid which does not involve drying and which the authors claim gives a more accurate differential count of abnormal forms than the methods now commonly used. A working classification of abnormal forms is suggested.

On the basis of the findings of 236 specimens examined according to the methods described in this paper, minimal values of the four main factors in semen analysis (density, morphology, motility and viability) which are thought to be compatible with adequate fertility are suggested. The authors are of the opinion that male subfertility does not become of primary importance unless the results of the semen analysis are found to fall below the minimal values in all four factors (about 20 per cent of their cases), and is of relative importance when the values fall below the minimum in at least two of the factors (about another 40 per cent of their cases). It is stressed that the relative importance of the male factor in any particular subfertile marriage cannot be properly assessed without a complete semen analysis.

Repeated seminal examination of the same subject shows that although the semen may vary (effects of recent coitus, of long periods of continence and other factors) there is a tendency for the individual to produce a characteristic sperm picture. Some evidence was obtained which suggests that the fully fertile man can replace his available sperm population very much more rapidly than a subfertile man, and that the examination of a second specimen within 24 hours of the first may provide a delicate test of a man's degree of fertility and his response to treatment.

The results of treatment of 11 men were disappointing as indicated by examination of the semen.

(This paper should be of interest to all those interested in the study of sterility, and this has come to mean chiefly gynecologists. In spite of the great frequency of the male factor in the causation of sterility, it appears to me that urologists as a group have exhibited comparatively little interest in this aspect of the problem, concerning which there is still so much that we do not know. In many communities the gynecologist is of necessity obliged to include semen examination as a part of his own sterility work. Very little has been accomplished in the matter of treatment of seminal deficiencies, aside from general treatment and perhaps thyroid therapy in some cases. Certainly no one can be enthusiastic about the results obtained through the employment of chorionic and other gonadotrophins often prescribed in such cases.—Ed.)

## BASAL TEMPERATURE GRAPHS: AN AID IN THE STUDY OF STERILITY

PENDLETON TOMPKINS

Clin. Med., 52: 309-310, 1945

In recent years it has been reported that the time of ovulation can be calculated with considerable accuracy from graphs of the daily basal body temperature, taken in the morning before rising, eating, drinking or smoking. It has

been found that usually the temperature is relatively low immediately after menstruation, and remains low until about 2 weeks before the next period. At this time the temperature shifts abruptly to a lower degree, often dropping one or two-fifths of a degree from the previous level. The next day it rises three or four-fifths of a degree and remains high until a day or two before menstruation when it falls to the lower level. The low-to-lower-to-high shift is assumed to take place at or about the time of ovulation. If the patient becomes pregnant the temperature will continue at the high premenstrual level for many weeks. Graphs drawn on the grid-forms designed by the author for patients' use are used to illustrate the characteristics of the normal temperature curve throughout the cycle and to exemplify their usefulness to the infertile couple in pointing out the time of maximum fertility.

(The subject of basal temperature graphs as an aid to the study of sterility was commented upon rather fully in connection with another paper by the same author, abstracted in the February issue of the *Survey* (p. 96).—Ed.)

## OVARIAN FUNCTION AND BODY TEMPERATURE

I. HALBRECHT

*Lancet*, 249: 668-669, 1945

This paper describes an attempt to assess the reliability of the waking body temperature as an indicator of ovarian activity in sterile women and women suffering from amenorrhea, polymenorrhea and premature menopause. The material consists of the daily waking temperature records of 130 more or less regularly menstruating sterile women throughout 270 menstrual cycles. In 199 cycles the curves were found to be definitely biphasic, the mean differences in temperature between the two phases being 0.5 to 0.9°F. In 39 cases the cycles were less decisively biphasic, with differences of less than 0.5°F. between the temperatures in the estrin and progestin phases. In a few cases there were four phases instead of two, but whether this was due to two ovulations in the same cycle was not determined. In 33 cases (12 per cent of the cycles recorded) the cycles were monophasic. A group of amenorrheic patients all showed monophasic cycles over one to three months. The abrupt fall of the temperature to the lowest level of the estrin phase coincided with the onset of menstruation in 100 cases; in 52 it preceded the onset of the flow by one to three days and in 45 cycles the progestin high level continued one to four days after the onset of menstruation. Of 40 women who became pregnant, 37 showed a constant high temperature level (98.6 to 99.3°F.). In three cases the temperature fell below 98.6° in the second or third months of pregnancy. In two cases of habitual abortion the temperature curves recorded from the beginning of pregnancy showed a sudden fall below 98.6°F. several days before the onset of the abortion.

Treatment with extract of pregnant-mare serum or with low-dosage irradiation

tion was started in 20 cases in which failure of ovulation seemed to be the main cause of sterility. Before treatment the temperature curves were monophasic. Two of the six patients treated by low-dosage irradiation and two of those treated with pregnant-mare serum showed a change from the monophasic to the diphasic type of cycle immediately after the treatment.

## TREATMENT OF INFERTILITY IN MALES

NORVELL BELT

Med. Ann. District of Columbia, 14: 450-451, 1945

The war has presented a most unusual opportunity to study the problem of infertility by virtue of its many marriages and exigencies of impregnation before servicemen went overseas. The author describes the method and results in treating 600 men. The prognosis in male infertility is improving although many factors remain unsolved. At present there is a 46 per cent chance of success.

The routine in this series of cases consisted of a history, physical examination and complete sperm evaluation followed by special tests when indicated. The duration of the apparent sterility, pregnancies by previous marriages, use of contraceptives, diseases, operations, injuries and anomalies are important in the history. A general physical examination with special attention to constitutional diseases, endocrinopathy and nutritional deficiencies is followed by minute examination of the genital system. The sperm evaluation includes the volume, pH, sperm count per cc., percentage of active sperm, survival time and morphologic study. Normal findings were revealed in about 10 per cent of the husbands and the remainder were subjected to treatment.

The type of treatment consisted of hormone therapy, prostatic massage, removal of all obvious pathology and a careful program of rest, diet, regulation of habits and exercise. The average length of treatment for each patient was 3 months. In this series there resulted 273 pregnancies.

Factors contributing to success appeared to be: (1) an increase in the sperm count, usually to above 50,000,000 per cc. with 50 per cent or more active; (2) correction of abnormal morphology; (3) increase in volume of ejaculate to 3 cc. or more; (4) endurance time of sperm activity was at least 5 hours in successful cases; and (5) treatment of testicular tuberculosis, prostatitis and urethral stricture. Analysis of unsuccessful cases revealed the following: (1) a large number had a history of protracted febrile diseases; (2) bilateral atrophy of the testes following mumps was present in 19 cases; (3) gonococcal epididymitis was present in only 3; (4) sex habits were abnormal in 6 cases; (5) renal pathology existed in 2 cases; (6) occupational exhaustion was present in 180 cases.

The author mentions as significant in the successes, the increase in number of active sperm. Bilateral mumps has been overemphasized as a cause of infertility. Prostatitis, urethral stricture and febrile illnesses are factors pertinent to impaired fertility. Nutritional disturbances cause infertility and often can be corrected. Three out of 7 patients having nutritional disturbances responded to administration of amino acids and vitamins.

## DEATH FROM AIR EMBOLISM FOLLOWING INSUFFLATION DURING PREGNANCY

HERBERT S. BREYFOGLE

J. A. M. A., 129: 342-344, 1945

Since 1936 three deaths directly attributed to insufflation of the vagina during pregnancy have been reported, one from Canada and two from England. The author presents, in this report, a fourth case and the first to be recorded in medical literature in this country.

A 21-year-old woman was brought to the hospital from the office of an osteopath and pronounced dead on arrival. She had consulted the osteopath because of an irritating vaginal discharge. The osteopath began to insufflate the vagina with silver picrate compound powder, 1 per cent silver picrate in kaolin, using a Shelanski insufflator. Shortly after the conclusion of the treatment the patient became dyspneic, cyanotic and unconscious, and a white froth began to exude from the mouth. From twenty to thirty minutes later she expired.

Autopsy diagnoses were as follows: Primary: Gas bubbles in right auricle and ventricle, edema and congestion of the lungs, hemorrhagic infarct of the lower lobe of the left lung, pregnant uterus containing normally implanted fetus, discoloration of vaginal mucosa and subpleural petechiae. Accessory: infarct of right kidney, adrenal rests of kidneys and polyp of ascending colon.

The clinical picture in this case strongly suggested acute fulminating anoxia. It was calculated that about 925 to 2,200 cc. of air was injected into the vagina. The potential capacity of the vagina is assumed to be about 1,144 cc. This would imply that at least 500 cc. or more of air was forced into the pregnant uterus within a brief interval of time, thus providing the necessary requisites for air embolism to result. It was supposed that the air entered the systemic venous circulation at the site of the placental implantation and was carried directly to the right auricle and ventricle of the heart.

The facts brought forth by a study of deaths resulting from vaginal insufflation during pregnancy indicate that it can be an extremely dangerous procedure, especially in the latter half of gestation. Multiparity also appears to be a factor adding to the risk. Since other methods are equally effective in the treatment

of trichomoniasis, it appears that insufflation of the vagina may be abandoned. 13 references.

(A sufficient number of cases of this sort have now been reported to make clear that the widely employed insufflation method of applying various powders to the vaginal wall in the treatment of trichomonas vaginitis is associated with a definite risk of air embolism in pregnant patients. As the author states, there are other effective methods of applying trichomonicidal medicaments, and no one should wish to take the risk imposed by the insufflation technique.—Ed.)

## MISCELLANEOUS

### PELVIC AND ABDOMINAL PAIN IN WOMEN

CHARLES A. GORDON

Rev. Gastroenterol., 12: 353-356, 1945

The author discusses the diagnostic values of abdominal or pelvic pain, the difficulties encountered in determining the localization of pain, differences between pain and tenderness, and differences in individuals to tolerate or describe pain. Descriptions of pain are generally not very accurate. Valid conclusions as to the intensity of pain depend upon the extent of its interference with the patient's daily activities and interests, appetite, sleep and her ability to concentrate attention upon her environment. Transient loss of consciousness, syncope, pallor, sweating and collapse usually indicate severe pain as in spreading peritonitis, perforation of the sigmoid following its invasion by ovarian carcinoma and rupture of ovarian abscess or tubal pregnancy. The extent of muscular rigidity is not necessarily an essential finding as the abdominal wall may be soft in cases of gangrenous intestines late in peritonitis or when the peritoneal cavity is filled with blood from ruptured tube or uterus.

Pain is largely of peritoneal origin, arising from mesentery or from parietal peritoneum, although the stimulus may actually originate in its subserous tissue. It is generally accepted that the solid viscera are insensitive to pain and that the hollow muscular-walled viscera respond to stretching and contraction. However, occasional variations in individuals occur. Stretching of the uterus by multiple pregnancy, hydramnios or large fetus may give rise to pain, and Braxton-Hickes contractions, which are typically not painful, may become severe enough to send the patient prematurely to the hospital for delivery.

The severity of the pain alone is not an index to the serious nature of visceral pathology. Cancer of the reproductive organs commonly causes no pain until the pelvic peritoneum has been invaded. Dysmenorrhea may become very severe although no visceral lesion can be demonstrated.

A common complaint of women is pain in the ovary although it is not possible to feel definitely that pain is in any particular organ, the ovary is not always in the same place in the same individual, and the pain stimulus does not arise in the ovary as this organ is not covered with peritoneum.

Anxiety neuroses and phobias accompanied by abdominal pain and pain of extragenital origin present diagnostic difficulties. Epigastric pain, often severe and paroxysmal and referred to the back and lower ribs, independent of food and often recurring at definite intervals may be seen without any anatomical basis discoverable by x-ray. Abdominal pain may be due to loosening of the pelvic girdle. Since physiological relaxation occurs during pregnancy and

probably also during menstruation, trauma, posture, housework or parturition may cause sacroiliac strain with anterior abdominal pain as well as backache.

Fibroids of the uterus typically cause no pain, but under certain conditions, such as the expulsion of a submucous fibroid, they may cause painful rhythmic contractions of the uterus.

## PELVIC PAIN: ITS ETIOLOGY AND TREATMENT

D. M. SATUR

Jour. Indian Med. Assoc., 14: 195-199, 1945

After a brief survey of the state of knowledge concerning the innervation of the female genital organs, the characteristic features of visceral pain are given: (a) It is usually deep-seated and of a dull, heavy character. It may, however, be intermittent or spasmodic; (b) It is imperfectly localized; in the case of the uterus the pain may be central, unilateral or bilateral; (c) It is unaffected by movement and unaccompanied by tenderness or muscular rigidity. The characteristics of referred pain are given as: (a) It is superficial, sharp or stabbing in quality, as in sudden rupture of an ectopic pregnancy; (b) It is continuous, accurately localized and aggravated by movement; (c) It is accompanied by tenderness and rigidity of the abdominal muscles. The site of referred pain depends on the site of irritation of the peritoneum.

In the author's experience the manifestation of pain in the iliac fossa was more frequently on the left side than on the right, and was aggravated by constipation. The theory is advanced that this might be attributed to the movement in the loading and unloading of the rectum.

Benign or malignant tumors of the uterus, cancer of the cervix, malignant tumors of the ovary, chorionepithelioma, or retrodisplacement of the uterus, usually do not of themselves cause pain, but may cause severe pain if complicated by peritoneal irritation, torsion, adhesions, or involvement of other organs. Carcinoma of the body of the uterus gives rise to pain earlier than does cancer of the cervix. This may be due to painful spasm of the uterine muscles. Ovarian cysts usually give rise to pressure symptoms, but there may also be a dull, dragging pain in one or both iliac fossa. Severe pain is experienced if axial rotation occurs. Endometrioma of the ovary with chocolate cysts is characterized by pain either in the lower abdomen or back. Premenstrual and menstrual dysmenorrhea are marked and dyspareunia may be present. If endometriosis has involved the rectovaginal septum, pain on defecation is also experienced. The most constant feature of ectopic pregnancy is abdominal pain. Chronic tubo-ovarian inflammation gives rise to pain in the lower abdomen, combined with backache, which is aggravated by exertion, menstruation and constipation.

## NASOGENITAL RELATIONSHIP. REVIEW OF THE LITERATURE

RAYMOND S. ROSEDALE

Arch. Otolaryngol., 42: 235-238, 1945

The scantiness of the indexed literature on the relationship between the nose and the genital organs is attested by the fact that only twenty-five studies are described in this paper. Of these studies, nine are reports of clinical observations on nasal manifestations (changes of secretions, odor of ozena, etc.) during menstruation and pregnancy. The others, summarized very briefly, deal with experimental work as follows: (1) on animals, designed to test the effect of extirpation of the olfactory bulbs or inferior turbinates on sexual desire and on the development of genital organs; (2) on animals and human beings, to determine the effects of administration of silver nitrate or estrogens into the nasal areas on pseudopregnancy; and (3) on changes in the nasal tissues following castration or hormone therapy. No synthesis is made of the findings and no definite conclusions are drawn by the author.

## RESULTS OF VARIOUS TYPES OF TREATMENT IN ADENOCARCINOMA OF THE ENDOMETRIUM

CHARLES E. McLENNAN

Am. J. Obst. &amp; Gynec., 50: 254-62, 1945

During the years 1928 to 1943, inclusive, 225 women with carcinoma in the body of the uterus were observed in the University of Minnesota Hospitals. In this report, these patients have been divided into two groups: 111 who were seen more than five years ago and whose treatment may be judged on a five-year basis, and the remainder who were seen during the last five years. None of the entire series has been lost in the follow-up program.

Only 80 of the 111 patients seen five years ago were treated exclusively at the University of Minnesota Hospitals. More than half of these (46) were treated with irradiation alone (radium and/or x-ray). The chief reason for not performing hysterectomies on these patients was actual or possible extension of tumor beyond the body of the uterus. Only 22 per cent of this group receiving irradiation alone survived more than five years.

Twenty-nine other patients were treated with various combinations of hysterectomy with radium or x-ray or both. In this group 83 per cent were cured. Although the irradiated group contained all the surgically "bad risk" patients, the author believes, in retrospect, that perhaps some of these could have stood operation successfully. He has found that certain patients treated by irradiation alone may be salvaged many years later by hysterectomy for recurrent or persistent carcinoma.

Apart from the 111 five-year patients were 114 handled after January 1, 1939. Only 53 per cent of these patients have been able to go through a planned, standardized routine of treatment. About 70 per cent have received what might be termed adequate treatment, in the sense that total hysterectomy was performed. Between 50 and 70 per cent of the 114 may be said to have a chance of survival on the basis of the treatment instituted when first seen.

Only one of the 114 patients seen during the last five years has died of carcinoma. Only one-fourth of the patients receiving incomplete therapy have survived from 0 to 4 years.

The operative mortality for the entire series of patients has been 5.8 per cent, unless 3 patients with virtually hopeless prognosis prior to operation are excluded, when the over-all rate becomes 3 per cent.

Hysterectomy generally is conceded to be the important part of the therapy for carcinoma of the body of the uterus. The question of whether the preoperative addition of x-ray and/or radium will materially increase the survival rates in operable cases as yet is not completely answered. The use of irradiation should be followed, whenever possible, with hysterectomy. It is suggested that preoperative deep x-ray therapy will add nothing to the ultimate cure rates. No conclusions can be drawn as yet from recent experience with intra-uterine radium followed in 4 to 6 weeks by hysterectomy.

The final results in the treatment of carcinoma of the uterine corpus are predetermined to a considerable extent by the nature of the material presented for therapy, in terms of metastases, medical and surgical complications, age, weight and nutritional status. 9 references.

(While the treatment of adenocarcinoma of the uterine body must still be considered to be in a fluid, transitional stage, the growing consensus is that irradiation, followed after an interval of usually about six weeks by radical removal of the pelvic organs, is the method of choice. The author's results with irradiation alone support the growing feeling that this alone is not enough to cure most cases, and that hysterectomy is an essential part of the management.—Ed.)

## METASTATIC ADENOCARCINOMA OF THE CERVIX UTERI ASSOCIATED WITH PRIMARY GASTRIC CANCER

EDWIN L. WILLIAMS

*Am. J. Obst. & Gynec.*, 50: 342-44, 1945

It is now well known that the "Krukenberg tumor" represents secondary carcinoma of the ovary associated with a primary colloid carcinoma of the gastrointestinal tract usually occurring in the stomach. The ovary has uniformly been the seat of the secondary lesion. It is the purpose of this paper to describe a carcinoma of the cervix uteri occurring in association with a carcinoma of the cardiac portion of the stomach.

A 32-year-old multipara was admitted to the hospital with the chief complaint of persistent vomiting which had begun about 10 months previously. During this time she had lost 125 pounds. She complained of pains in the lower abdomen and mild dysmenorrhea.

General physical examination revealed no other significant findings than weight loss. On pelvic examination, the cervix, anterior vaginal wall and fornices of the vagina were felt to be of a "woody" consistency.

Esophagoscopy revealed a dilatation of the entire esophagus, marked hyperemia of the esophageal wall, and an obstruction at the level of the diaphragm. Cystoscopy revealed hyperemia of the bladder wall. Gastrointestinal roentgenology was negative.

An exploratory laparotomy was performed. Examination of the stomach revealed a nodular mass high on the lesser curvature extending into the esophageal hiatus. Nodules were scattered over the peritoneal surface of the diaphragm, lateral pelvic walls of the peritoneum, and on the surfaces of the ovaries, the omentum and the fundus of the uterus. A gastrostomy was performed and the abdomen closed. The patient's immediate course was uneventful.

Microscopic sections from the gastric lesion, the peritoneal metastases and the cervix presented strikingly similar characteristics. 3 references. 2 figures.

The case hence shows that adenocarcinoma of the cervix may occur in association with a primary gastric cancer.

(An examination of the two illustrations accompanying this paper would seem to leave little doubt that the carcinoma of the cervix is, as the author believes, of metastatic and not primary type; in other words, that the case is not one of multiple carcinoma. The section from the cervix even shows a number of typical "signet" cells, like those seen in Krukenberg tumors of the ovary. In this case the ovaries were said not to have been enlarged, though there is no note as to their microscopic examination. Since they are said to have shown surface involvement, and since they were adherent to the surface of the broad ligament, a logical route of lymphatic permeation to the cervix would suggest itself. I have seen one case in which uterine curettage yielded a large amount of ovarian cancer tissue as a result of the penetration of the uterine wall by an advanced ovarian carcinoma which was welded to the uterus.—Ed.)

## FATAL PERITONITIS FROM PROCTOSALPINGOSTOMIC FISTULA COMPLICATING LYMPHOPATHIA VENEREUM

ALEXANDER E. PEARCE, JOHN O. BOWER AND JOHN C. BURNS

Amer. Jour. Surg., 69: 496-498, 1945

The case presented in this paper is notable primarily for the circuitous route which the lethal rectal contents took before inducing the fatal termination. The patient, a 32-year-old Negress, was admitted to the surgical service at the Philadelphia General Hospital because of diffuse abdominal pain and vomiting. Prior to hospitalization she had taken several enemas and simultaneously passed

greenish feces and vomited greenish fluid. Pain in the left groin and radiating into the rectum had been present for five days prior to admittance to hospital. The abdomen was markedly distended but palpation revealed no masses. The anterior rectal wall was greatly indurated as high up as the fingers in the vagina could reach. Rectal examination revealed a stricture about two inches above the cutaneous margin. The provisional diagnoses were: (1) rectal stricture due to lymphopathia venereum; (2) peritonitis due to pelvic inflammatory disease; (3) syphilis, site undiagnosed; (4) hypochromic anemia; and (5) urethral caruncle. As perforation of the bowel was considered likely the patient was placed on an Ochsner regime and Wangenstein suction instituted. Urine analysis demonstrated 2 plus albumen, 2 plus leukocytes, 1 plus red cells and granular casts. Flat plate of the abdomen revealed a paralytic ileus with no definite evidence of obstruction. Three days after admission, signs of consolidation appeared in the left base, and the next day consolidation developed in the other base. Distention was unchanged and peristalsis was absent. The patient died the same day. At autopsy the rectum revealed advanced lymphogranuloma with a stricture two inches above the skin margin. Careful dissection demonstrated a fistula between the left side of the rectum, just above the stricture, and the left Fallopian tube near the ampulla. The uterine end of the tube was occluded. Extravasation of rectal contents was through the tract in the left broad ligament into the left Fallopian tube and into the peritoneal cavity.

## GYNECOLOGY IN INDUSTRY—CAUSES, TREATMENT AND EDUCATIONAL PROGRAM

HANNAH PETERS AND WILSON FOOTER

Indust. Med., 14: 755-760, 1945

For the past two years the Gynecology Clinic of the Permanente Foundation Hospitals has served a group of women comprising as many as 23,000 employed at one time in the shipyards in the Richmond (Cal.) area. Some of the problems were those commonly encountered in a gynecological clinic. Others were accentuated and these are summarized in this paper.

The menorrhagia and metrorrhagia which is frequently found in women when they start to do heavy work was found in this group of women. No correlation with the type of work they did was found, nor could any organic reasons for the complaints be found. It was found, however, that the caloric requirements and intakes of these women became greater when they began to do manual work. Their diet habits became such that they ate more and more carbohydrates, with the result that the more they ate the greater their vitamin B deficiency became. The first symptom these women showed was frequently a prolonged as well as an excessive menstrual flow. By injecting vitamin B complex intramuscularly the

authors were able to reduce the length and amount of flow to a normal period. In several cases which were followed by suction biopsies it was noticed that hyperplastic endometrium as well as persistent proliferative endometrium was changed into endometrium that underwent cyclic changes when vitamin B therapy was instituted. A detailed report of the cases treated with vitamin B complex will be published later.

Information about the effect of climbing, sweeping, riveting, heavy continuous lifting and similar work is not as yet available.

Many cases of abortion came to the attention of the clinic, but in no case could the type of work be held responsible for the early termination of pregnancy. No data are presented with reference to the number of induced abortions, but it is pointed out that the policy of discharging a woman as soon as it becomes known that she is pregnant accomplishes one of two things: (1) The woman will try to conceal her pregnancy as long as possible and not secure adequate prenatal care, or (2) She may try abortion. A sound maternity policy and a conception control program available to women workers are suggested as measures toward controlling abortion.

Cancer of the ovaries, uterus, and the cervix amounted to 0.9 per cent of all the new cases in the hospitals. This percentage remained the same for the two-year period. The approach to this situation was two-fold. 1. An attempt was made to find and utilize the best means of diagnosis. Each patient entering the clinic for any complaint whatsoever was examined with the specific aim of ruling out the existence of cancer of the reproductive organs or the breasts. 2. An attempt was made to disseminate information to the patient to the effect that a physical examination should be had every six months, and that any symptoms arising in the interval should be investigated promptly. The results of this program can not yet be evaluated.

Thirteen per cent of the patients were found to be infected with gonorrhea. Most of these were discovered incidentally during examination for other complaints. The most frequent picture was that in which the woman stated that she had a normal menstrual period which ended two weeks or even only a few days before a new period started. Smears and cultures taken in these cases often proved the presence of a gonococcal infection. Many problems of so-called "functional menorrhagia" were solved when smears and cultures were taken. It is pointed out that smears and cultures from a bleeding cervix can be adequately read and in the authors' experience have proven to be of great value. A venereal disease educational program for women is described.

(This report is illustrative of the intelligent health programs provided in an increasing number of our industries, for the benefit of the greatly increased number of women employees, especially during wartime. One of the most valuable parts of the work at the Permanente Foundation was that designed for the early detection of gynecologic cancer, under the direction of Dr. Footer. It is to be hoped that the post-war shrinkage in industry will not result in any curtailment in these programs for the gynecologic care of women in industry.—Ed.)

## ENDOMETRIOSIS OF THE UMBILICUS: CASE REPORT

J. CHASSAR MOIR

Proc. Roy. Soc. Med. (Sect. Obst. &amp; Gyn.), 37: 437-438, 1944

The patient, aged 47 years, complained that for three or four years she had had a slight discharge of blood from the umbilicus with each menstruation. This was accompanied by pain in that area. Menstruation was normal and not accompanied by any unusual lower abdominal pain.

On inspection, the umbilicus was found to be rather deep, and at the bottom there was a small brownish projection. Gynecological examination suggested some thickenings in the pelvis at the sides of the uterus. The patient was given instruction in the regular cleansing of the deep umbilicus, and told to report again at a later date. This she did; the symptoms were as before and she was therefore admitted to the hospital.

At operation the whole umbilical area was carefully resected; it was now obvious that there was an abnormal thickening of the region, but the inner or peritoneal surface of the umbilicus was quite smooth. An opportunity now presented to examine the pelvic organs, and it was found that they were involved in an extensive endometriosis with numerous areas of tarry blood cysts. There did not appear to be any communication between the pelvic endometriosis and the umbilicus. As the patient was already at the menopausal age, and as there were no symptoms relating to the pelvic organs, further operation was not thought justifiable and the abdomen was accordingly closed.

The patient made a good recovery and when seen six months later was in excellent health. Histological examination of the umbilicus showed numerous gland areas indistinguishable from uterine mucosa in the proliferative phase. Two and a half years later the patient reports that she is in good health, save for obstinate constipation, and is free from abdominal pain.

Novak states that some forty cases of endometriosis of the umbilicus have been recorded. Vartan (1937) has recently recorded two further cases in one of which there was a monthly discharge of blood. An umbilical endometriosis that not only causes pain and swelling but bleeds regularly each month is extremely rare and justifies the record now presented.

(As Moir states, the majority of cases of umbilical endometriosis cause periodic pain and swelling, but periodic bleeding is much less common. It is of interest to note that in his case the umbilical lesion was associated with pelvic endometriosis, though this is not by any means always the case. As a matter of fact endometriosis in this situation has often been cited as circumstantial evidence for the so-called celomic metaplasia theory as to the origin of endometriosis, since remnants of celomic tissue are an essentially normal finding in this area, and since there is often no co-existing pelvic endometriosis.—Ed.)

## REPORT OF TWO CASES OF PELVIC ACTINOMYCOSIS REPRESENTING THE HARD AND SOFT TYPES

J. L. BUBIS

Med. Times, 73: 227-234, 1945

The first patient whose detailed case report is given in this paper was a 26-year old married woman. When first seen in May, 1941, she complained of severe abdominal pains, temperature between 102-103°F, and loss of weight. The pyuria, dysuria and hematuria cleared up after two weeks of bed rest, but the intermittent pain, which was most severe in the lower left quadrant of the abdomen, and occasional black, tarry stools continued until she was admitted to hospital the following November. At this time a diagnosis was made of chronic infection from tuberculosis or endometriosis, and retroversion. At operation, a slightly enlarged chronic appendix, both ovaries and both tubes were removed. The microscopic diagnosis included slight chronic appendicitis; bilateral chronic granulomatous, subacute and acute oophoritis (marked) (actinomyces); chronic and subacute perisalpingitis and perioophoritis; and bilateral chronic subacute and acute salpingitis with hydrosalpinx. Sulfa drugs gave only temporary relief. No fungi were found in the vagina or rectal discharge on November 29th and the patient was discharged six days later. She was seen each month with complaints of abdominal pain, loss of weight, and a hard mass in the cul-de-sac of Douglass until readmission to hospital in February, 1942. Vaginal puncture of the mass yielded about 10 cc. of serous fluid, and an incision into it yielded some necrotic material which showed rectal mucosa on microscopic examination. In April, 1942, she developed an abdominal abscess which drained spontaneously through the old incision. The yellowish discharge contained many actinomycotic granules. In May she had a perirectal infiltration and a small nodule was felt on the posterior wall of the bowel. Several times during the following year she had profuse orange colored discharge or foul-smelling pus from the rectum, followed each time by relief of pain. By March, 1943, she had gained some weight but continued to complain of severe pain which was controlled by hot packs and sedatives. At this time she had several abdominal fistulae with board-like hardness of the abdominal wall. She gradually became worse and died in January, 1944. No autopsy was obtained. It is thought that the portal through which the infection entered and attacked the ovaries was primarily through the vagina and that the rectum was secondarily involved by a band of adhesions between the uterus and the rectum. The initial infection probably was obtained when she had bowel movements in the tall grass on a farm in Pennsylvania.

The second patient, a 34-year-old married woman, was admitted to hospital in February, 1943, with complaints of abdominal pain, vomiting, and marked loss in weight. Vaginal examination showed a typical frozen pelvis, with the uterus riding on a firm, smooth mass which extended half way to the umbilicus. Rectal examination showed hard, nodular masses anterior, to the left and also posterior

to the rectum. On vaginal incision and drainage a large amount of green, thick pus was obtained. Biopsy material of the mass showed acute and subacute cellulitis of the vagina. The bacterial report was many pus cells and gram-negative bacteria, few gram-positive and gram-negative cocci. The culture showed abundant growth of *Staph. aureus* of the hemolytic strain, with slight growth of yeast cells. The patient left the hospital February 25th, but was readmitted March 26th with the complaints of vomiting, increased weakness, pain in the lower left quadrant of the abdomen and constant vaginal drainage, fecal in character. Vaginal incision and drainage were again performed on April 1st, and a quart of foul-smelling green pus was obtained. Culture of the pus showed nonhemolytic streptococci, partly anaerobic. After treatment for peritonitis she left the hospital slightly improved on April 22nd, but was readmitted May 17th and died two days later. The clinical diagnosis was pelvic abscess and gangrenous peritonitis due to infection from the introduction of stem pessaries, pelvic malignancy or ruptured diverticula. The diagnosis made at autopsy included among a variety of conditions: chronic, subacute, and acute gangrenous salpingitis and perisalpingitis, oophoritis and perioophoritis bilateral (marked) (actinomycosis and intestinal flora); abscess of right ovary; chronic, subacute and acute gangrenous pelvic peritonitis (marked) with early acute generalized fibrinopurulent peritonitis; paralytic ileus; ascending pyclo-nephritis, right kidney, with multiple old and recent actinomycotic abscesses.

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# *Obstetrics*

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## PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

### THE MECHANISM OF THE HISTIDINURIA OF PREGNANCY

ERNEST W. PAGE

Am. J. Obst. & Gynec., 51: 553, 1946

Since Voge first noted the histidinuria of normal pregnancy in 1929, over 100 articles have dealt with this subject. These studies have shown beyond doubt that the iminazole compound excreted is actually l-histidine and that much larger quantities of this essential amino acid are excreted during pregnancy, at least from the eighth to the thirty-sixth week after conception, than in the non-pregnant state.

The only serious explanation of pregnancy histidinuria which has been advanced is that of Kapeller-Adler and her co-workers. In a series of articles she has shown that only the human species excretes histidine during pregnancy; that liver tissue removed from pregnant women at autopsy does not readily metabolize histidine, while liver specimens from men or non-pregnant women show marked histidase activity; and that the addition of 50 to 500 rat units of chorionic gonadotrophic hormone to ground human liver in vitro inhibits histidase activity. She believes, therefore, that the placental hormone which is produced only by the human species inhibits the normal metabolic breakdown of histidine by the liver, thus resulting in its excretion. More recently she has found that histidine disappears from the urine in pre-eclampsia. She attributes this to the fact that a large proportion of the histidine in pre-eclampsia is transformed by a tissue decarboxylase to histamine and that the latter may be a cause of the toxemia.

After citing certain objections to the Kapeller-Adler theory, the author notes that the histidinuria of pregnancy could be due to a "lowered renal threshold," that is, to an inhibition of the tubular reabsorption of histidine rather than to any change in histidine catabolism in pregnancy. If this were true, then the administration of histidine orally or intravenously should result in its excretion at normal or low blood levels. If the liver histidase were inhibited on the other hand, then the administration of histidine should result in a greater and more prolonged rise in the blood level. The present study is an examination of these two hypotheses.

Employing a carefully controlled technique and taking precautions against inherent errors in urine collection, the author found that there is a consistent difference between the blood histidine curves of non-pregnant and pregnant

women following the ingestion of 3 Gm. of this amino acid. In normal pregnancy the level rises more slowly, remains lower and persists for a longer period of time. However, the most significant finding was that a much higher rate of histidine excretion occurred at the same or even at lower blood levels in pregnant women. This could mean only one thing, namely, that there is a "lowered renal threshold," or in other words a diminished reabsorption of the amino acid by the renal tubules. When given by vein, histidine disappears from the blood stream with equal rapidity in both pregnant and non-pregnant women, a fact suggesting that there is no interference with its utilization or destruction during gestation. The highest excretion rate following intravenous administration was 262 mg. in one hour; this occurred in a normal pregnant woman and represented an excretion rate of 15 per cent of the histidine injected. The high excretion rates in pregnancy and the lowest rates in non-pregnant women were observed at the same blood levels, again indicating an alteration of the renal threshold.

On the basis of his experiments the author concludes that pregnancy histidinuria is due to an inhibition or interference with the renal tubular mechanism for this particular amino acid and is not the result of any hormonal inhibition of liver histidase.

(See Editorial Note following next abstract.—Ed.)

## A SHORT STUDY OF HISTAMINASE ACTIVITY DURING PREGNANCY

E. W. KOLOZYNSKI

J. Obst. & Gynec. Brit. Emp., 52: 486-495, 1945

Histaminase, first described by Best and McHenry, is an enzyme which inactivates histamine. Histamine, in turn, is formed in the intestine from the amino acid, histidine, and is widely distributed in the body.

The present investigations were concerned chiefly with the fluctuations of histaminase during pregnancy. The method employed was worked out from Kapeller-Adler's test based upon a qualitative method in which hydrogen peroxide, produced by the action of histaminase upon histamine, decolorizes the dye indigo disulphonate. A detailed statistical analysis is presented of the serum histaminase levels in 12 non-pregnant, 40 pregnant and 9 pre-eclamptic women. In the non-pregnant women no evidence of specific histaminase activity could be demonstrated. When, however, sera from normal pregnant women were studied, there was definite evidence of specific histaminase activity. Furthermore, the activity varied with the duration of pregnancy, being low in the first 100 days and high thereafter. These findings agree with those of others. This elaboration of an amine-oxidase, specific for histamine, within the body during pregnancy constitutes an interesting problem which quantitative measurement will assist in solving. The sera from patients with pre-eclampsia also showed histaminase activity and it was impossible to demonstrate any inhibition

of histaminase activity in this complication as has been claimed by Kapeller-Adler. However, the present author's observations in pre-eclampsia were avowedly not extensive.

A substantial portion of the article is devoted to details of methodology which will be of interest to chemists and of great importance to anyone who desires to carry out histaminase determinations. In this section of the paper Kolozynski presents data bearing on the disagreement as to the specificity of histaminase activity. He finds, in sum, that the sera from non-pregnant as well as pregnant women show amine-oxidase activity but that only a portion of this is specific for histamine. The non-specific fraction was found in about the same amount in pregnant and non-pregnant women and showed no tendency to increase during gestation. A method is described for determining specific histaminase activity and it is this fraction which manifests the remarkable alterations in pregnancy as described above.

(A large literature has developed over the past 15 years on the behavior in pregnancy of the 3 closely related substances, histidine, histamine and histaminase; and not a few competent observers believe that irregularities in the metabolism of these compounds play an important role in the production of many common obstetrical complications, such as toxemia, abruptio placentae, abortion and uterine inertia. The chain of evidence in support of these relationships is far from complete and is at points rather tenuous, but certain links appear to be irrefragable. All in all, enough truth seems to underlie the concept to indicate that its future development bears watching. The main features of the hypothesis may be recalled as follows:

*Histidine.* Histidinuria is so characteristic of gestation that several tests for pregnancy—the so-called "bromine tests"—have been based on the chemical demonstration of urinary histidine. Although these procedures have proved much less reliable than the hormonal tests and are not widely used, the fact that they are about 85 per cent accurate is clear evidence that histidinuria is one of the most constant alterations of pregnancy. As Page points out above, this phenomenon might be due either to some change in the metabolism of histidine during gestation or to a lowered renal threshold for the substance. The former of these explanations was brought forth by Kapeller-Adler in the late thirties and until the appearance of Page's paper has been rather widely held. It was her contention that chorionic gonadotrophin inhibits the action of the enzyme histidine carboxylase, the function of which is to break down histidine. With the efficacy of the enzyme impaired, it is easily conceivable that excessive quantities of histidine might accumulate and escape into the blood and urine. Page's study effectively disproves the Kapeller-Adler theory of histidinuria in pregnancy and puts it on the more reasonable basis of a "lowered renal threshold." The histidinuria of normal pregnancy may, therefore, be dismissed as without bearing on the metabolism of the histidine-histamine-histaminase complex.

But Kapeller-Adler has maintained also that in severe pre-eclampsia and in eclampsia the normal histidinuria of pregnancy disappears and she lays great stress on this finding. The sequence of events she pictures here is as follows: first, excessive activity of the enzyme histidine carboxylase results in a diminution in the amount of histidine in the body and its consequent disappearance from the urine; second, a flooding of the body with histamine occurs as the natural result of increased histidine catabolism; and third, decreased manufacture of histaminase ensues, consequent upon the noxious effect of the large amounts of histamine on the liver, kidney and other vital organs. In sum, the Kapeller-Adler theory regards the toxemias of pregnancy as a disturbance in the metabolism of the enzymes responsible for the formation and destruction of histamine.

In regard to the first tenet of this concept, namely, that histidinuria disappears in severe

pre-eclampsia and eclampsia, this observation need not necessarily be explained on the basis of excessive histidine destruction. Since the kidney in severe pre-eclampsia and eclampsia has difficulty in excreting other substances, it may well have difficulty in excreting histidine and hence the absence of histidinuria in these conditions may be renal rather than metabolic. This is surely a weak link in the chain, but let it be observed that it is an unneeded link, since even with a normal rate of histidine breakdown and histamine production, any substantial reduction in histaminase might conceivably flood the organism with histamine. This brings us to the possible roles of histamine and histaminase in normal and pathologic pregnancy.

*Histamine.* If I am not mistaken, the first suggestion that histamine intoxication may cause toxemia of pregnancy came, not from an obstetrician, but from the eminent British physiologist, E. H. Starling, who commented as follows: "Our recent experiments show that the vasomotor center is acutely sensitive to the slightest alteration in the blood flow through it. The smallest increase in this flow causes vasodilatation and therefore a fall of blood pressure, while the slightest decrease brings about general vasoconstriction and a rise of blood pressure, and these effects are permanent—that is, last as long as the alteration which is effected in the vasomotor center. All the mechanisms for the regulation of the activities of the heart and arteries are directed toward the maintenance of a blood flow through the capillaries in accordance with the needs of the tissues they supply. First among these needs are those of the vasomotor center and brain. There is evidence that in many parts of the body—perhaps in all—the capillaries are endowed with contractility, and this properly must be a considerable factor in regulating the irrigation of the tissues according to their activities. Any such contraction of the capillaries to the vasomotor center would evoke an immediate response and rise of arterial pressure lasting as long as the contraction of the capillaries. But we know that the capillaries are susceptible to other chemical influences which alter their permeability—that is, the amount of blood fluid which filters through their walls. A familiar example of such a change is the wheals produced in the skin as a result of the injection of certain animal poisons or by the local injection of substances such as histamine. Any similar change in the capillaries to the brain would be fraught with evil results for the circulation through them; for it must be remembered that these capillaries run in a pericapillary lymphatic; increased exudation would cause a rise of pressure in the lymphatic and a corresponding narrowing of the lumen of the capillary. I would suggest that such a condition of altered capillary wall is responsible for the high arterial pressure which is the invariable concomitant of certain toxic conditions such as uremia and the toxemia of pregnancy. In both of these, the high pressure I have ascribed to interference with the capillary circulation to the vasomotor center is accompanied by well marked signs of deficient circulation through other parts of the brain, such as headache, amaurosis, temporary loss of speech, various paralyses, and convulsions; and we know that in the toxemia of pregnancy at any rate, all these symptoms may subside with the termination of the pregnancy." (Brit. M. J., 1925, No. 3390, Page 1163; quoted by Hofbauer, *Am. J. Obst. & Gynec.*, 12: 159-189, 1926.)

The chief proponent of the histamine theory of toxemia has been Hofbauer, who has stoutly maintained for many years that histamine intoxication is the immediate cause of abruptio placentae and plays a major role in the production of pre-eclampsia and eclampsia. As may be seen in his recent article, "The Evolution of the Biologic Concept of the Etiology of Late Toxemia," (*Am. J. Obst. & Gynec.*, 51: 514, 1946) and in his earlier monograph, "Experimental Studies on the Toxemias of Pregnancy—Can Histamine Poisoning be Regarded as the Etiologic Factor?" (reference above), he supports his views not only by work of his own but by a vast array of evidence from the literature. As for the source of the histamine, he reminds us that during pregnancy the shedding of syncytial buds occurs from a chorionic surface which at term measures 6.5 square meters, obviously, a potential source of protein-split products such as histamine.

At first glance, the fact that histamine is known to cause a marked fall in blood pressure would seem to rule it out as a cause of the hypertensive toxemias of pregnancy. The above

quotation from Starling explains how histamine might conceivably cause hypertension and there is other evidence suggesting that under certain circumstances this substance may evoke constriction of the arterioles. However this may be, to most obstetricians histamine intoxication will fit in better as a cause of abruptio placentae than of toxemia. In the first place, histamine is a potent protoplasmic poison with special predilection for blood vessels (Hueper, W. C., and C. T. Ichniowski, *Am. J. Path.*, 20: 211, 1944). Anyone who has ever observed the utero-placental apoplexy of Couvelaire with its widespread hemorrhages must have suspected that such extensive rhexis of the blood vessels had been preceded by some kind of injury to the arteriolar and capillary walls, such as histamine might produce. In the second place, inasmuch as histamine (which was first isolated from ergot) exerts a powerful stimulating effect directly on the myometrium, it might well be responsible for the ligneous state of the uterus in abruptio. Thirdly, this amine produces profound shock; and finally, the studies of Hofbauer indicate that a very good replica of abruptio can be produced by injecting histamine into experimental animals.

Although the above circumstances are suggestive, it is only when they are supplemented by the more recent work on histaminase that the evidence becomes in any degree convincing.

*Histaminase.* In 1930 Best and McHenry (*J. Physiol.*, 70: 349, 1930) showed that simple saline extracts of various animal organs when used fresh and untreated, had the property of destroying the histamine in a solution to which they were added. They reported a method of extraction and assay of the histamine-inactivating substance and called it "histaminase" because of its enzyme-like properties.

During pregnancy, as attested by the study of Kolozynski above and others, serum histaminase increases greatly. According to Ahlmark (*Lancet*, 247: 406, 1944) this alteration begins very early and even after one month the enzyme activity of the serum in respect to histamine is about 100 times greater than in the non-pregnant state. He found it possible, moreover, to demonstrate an increase from one day to another and in different women the increase was remarkably constant. During the later part of pregnancy the histaminase activity of the serum is said to attain about 500-100 times the normal, varying somewhat from woman to woman. Moreover, according to Werle and Effkeman, as well as Kapeller-Adler, (*Arch. f. Gynäk.*, 170: 82, 1940; *Biochem. Jour.*, 38: 270, 1944), the histaminase reaction is specific with regard to histamine and can only be demonstrated in sera from pregnant women. In the opinion of some observers the histaminase content of the serum is diminished in pre-eclampsia and very low in abruptio placentae, but it will be noted that Kolozynski was unable to find any change in his 9 cases of pre-eclampsia.

The general, off-hand implications of the above findings are, of course, plain enough. It is hypothesized that in normal pregnancy a nice balance exists between histamine production and histaminase. By the same token, the tremendous increase in serum histaminase which occurs in pregnant women suggests a greatly augmented manufacture of histamine—presumably from chorionic villi. As long as this balance is maintained, everything goes well. If, however, histaminase in the blood and tissues diminishes, histamine gets the upper hand and causes various complications: toxemia, abruptio placentae, abortion, etc. If, on the other hand, histaminase for some reason is present in increased amounts, uterine inertia results because too much of the oxytocic histamine is destroyed. (See Danforth, D. N., and F. Gorham, *Am. J. Physiol.*, 119: 294, 1937.)

The two most important findings which have developed in the histaminase work have been the observations that histaminase increases many-fold in pregnancy and that this alteration is peculiar to pregnancy. The former of these appears to be well established and if the latter can be confirmed, this set of circumstances would surely indicate that histaminase plays some important role in normal gestation and possibly also in complicated pregnancy. However, there are several reasons for believing that the histamine-histaminase concept as a whole must still be regarded as an hypothesis only. In the first place, it has not been established that histamine is the causative agent in any pathological condition either in pregnant or non-pregnant persons. Second, a similar body of evidence was built up a few years ago to show that an excess of histamine causes various allergic conditions;

and histaminase was even marketed as a prophylactic and therapeutic agent for these states. But further investigation has shown that these claims lacked a factual basis. Third, the administration of histamine to animals for a period of some weeks has no effect upon the histaminase content of the tissues. It would be expected that increased need for histaminase would cause an increased production of the enzyme, particularly over a long period. Furthermore, although attempts have been made to protect guinea-pigs against anaphylactic and histamine shock by means of histaminase injections, these efforts have proved completely unsuccessful (Best and McHenry, *Canad. Med. Assoc. Jour.*, 43: 163, 1940). Finally, the evidence that serum histaminase undergoes any change in toxemia, abruptio or other obstetrical conditions, is scanty and in some instances conflicting.

There are thus two sides to the question; but it is an appealing problem upon which further work will be anticipated with interest.—Ed.)

## MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

### DIET REGULATION AND CONTROLLED WEIGHT IN PREGNANCY

W. J. DIECKMANN, DOROTHEA F. TURNER AND BARBARA A. RUBY

Am. J. Obst. & Gynec., 50: 701-12, 1945

The authors discuss the relation between diet and maternal and fetal complications and mortality. The data so far reported in the literature indicate the value of a proper diet. According to these data, some of the results of a proper diet are to prevent or decrease the incidence of abortion, anemia, toxemia, prematurity, fetal abnormalities, stillbirths and neonatal deaths, and to increase the mother's ability to nurse her baby.

The authors believe that a diet containing sufficient amounts of the essential foods, especially protein, vitamins and minerals, will lower the incidence of anemia in pregnancy, increase the resistance to infection during pregnancy or the puerperium, and also reduce the amount of edema in certain types of toxemia through weight control. They do not know whether or not such a diet will have any or all of the results mentioned in the preceding paragraph and believe that more extensive studies are necessary before changes are made in prenatal care. Prenatal care in both private and clinical practice is very expensive and additional dietary regulation would increase the cost for both the institution and the patient. The purpose of this paper is to examine critically the previous reports to see whether such added expense would be justified.

It has been reported that two-thirds of spontaneous abortions are associated with extensive anomalies of the fetus. The remainder are due to maternal causes, such as: anomalies of the uterus, tumors, systemic disease, abnormal implantations of the ovum, etc. Improper diet may be an important factor in the etiology of these causes, but positive proof is lacking. In the authors' studies, 2.4 per cent of the control group aborted and none aborted in the 3 complemented diet groups.

Pre-eclampsia occurs most frequently in the first pregnancy and diet is certainly one factor. The fact that it rarely recurs indicates that there are other factors because the diet would probably be the same in subsequent pregnancies. The authors found, in their complemented diet studies, a significant decrease in the incidence of toxemia in 2 groups and an increase in the other group. The inconsistencies were attributed to the small number of patients in each group.

If one uses pregnant standards, 12 per cent of pregnant patients are anemic. Bethell has shown that an intake of 50 grams or more of animal protein per day prevents the development of macrocytic anemia.

The majority of cases of abruptio placentae are associated with toxemia and it is conceivable that the toxemia could be attributed to diet.

It is difficult to see how a proper diet could be an important factor in reducing stillbirths and neonatal deaths.

Heredity is the important factor in the production of minor fetal anomalies and major anomalies have an unknown etiology. Animal experimentation has demonstrated that *extreme* diet deficiencies result in some animal species in fetal abnormalities.

Burke and co-workers believe that they have been able to increase the weight and length of the baby by increasing the protein intake.

A marked and prolonged deficiency in calcium, phosphorus and vitamin D before and during pregnancy will result in fetal rickets and faulty tooth development, as well as osteomalacia in the mother.

The quality of human milk has been shown to be affected by a deficient diet.

The authors believe that there is no need for a total weight gain greater than 8 kilograms above the ideal weight. The pregnant patient must have a proper diet but not an unlimited caloric intake resulting in excessive weight gain.

The increased requirements for lactation, over the needs of pregnancy, may be met simply by including an additional pint of fluid milk, an additional serving of citrus fruit and 2 tablespoons of peanut butter or equivalent.

The authors plan to make an evaluation of dietary instruction by an extensive study of a group of patients through a correlation of the dietary intake with the laboratory and clinical findings. They believe that research projects in maternal nutrition should be started in various clinics throughout the country so that in a short time, sufficient material will be available.

(Although it occupies only a line or two in the above abstract, the reader should note particularly the recommendation of Dieckmann and his associates that weight gain should be limited to 8 kilograms, or about 18 pounds. The more one practices obstetrics the more is one convinced that excessive weight gain in pregnancy is the cause of no end of complications, both major and minor. To keep weight gain down to 18 pounds may be difficult in many cases and will demand careful and expert dietary control in all, but is an end much to be desired—Ed.)

## THE TWO-HOUR PREGNANCY TEST

H. S. KUPPERMAN AND R. B. GREENBLATT

South. M. J., 39: 158-65, 1946

Employing the hyperemia-inducing effect on the ovary of gonad-stimulating substances in the urine of pregnant women as the basis of the reaction, the authors describe a 2-hour pregnancy test utilizing the immature female rat as the test animal. The unconcentrated urine is administered by intraperitoneal injection. The percentage of accuracy of the test (excluding the observations in ectopic pregnancy) proved to be 99.5 per cent in a total of 752 tests performed on 1346 rats. Comparison of the 2-hour pregnancy test with the Friedman test in a

series of 251 cases showed the rat test to be 100 per cent accurate in this series as compared with 97.3 per cent accuracy with the rabbit procedure. It was found that the hyperemic procedure was also adaptable to the immature hamster and adult female mouse, provided that 15 hours elapsed between the time of injection of urine and examination of the ovaries. Neither guinea pigs nor immature female mice could be satisfactorily adapted to the hyperemia end-point for the diagnosis of pregnancy. Observations on the hormone responsible for the ovarian hyperemia indicated that this reaction is dependent upon luteinizing or luteotropic activity of the administered urine. Employment of the 2-hour test in cases of suspected ectopic pregnancy showed that in a total of 18 cases, a correct diagnosis was attained in 83.3 per cent.

The advantages of the 2-hour test are enumerated by the authors and its lack of encumbrances, as compared with other diagnostic tests for pregnancy, is evaluated.

## ELECTRICAL DELIVERY

FRÉDÉRIC BENOIT

Gynéc. et obst., 44: 202-08, 1945

The author describes the technique of electrical delivery as follows:

1. Electricity is applicable only in normal deliveries; cases of true dystocia should be excluded.
2. Preliminary obstetrical examination is necessary to assure that labor is truly established, to ascertain the condition, size and position of the fetus as well as the pelvic dimensions of the mother, and to establish, as far as possible, the prognosis.
3. Artificial rupture of the membranes; this obstetrical procedure creates conditions favorable to a rapid delivery and is easy and without danger if executed correctly.
4. The best moment for application appears to be at the beginning of dilatation for multiparas and at a dilatation of 5 francs for primiparas.
5. The author gives a preparatory intramuscular injection of one ampule containing:
  - Posterior pituitary: 1 physiological unit (to sensitize the uterus).
  - Morphine: 1 cgr. (to block the higher pain centers).
  - Magnesium hyposulfite: 1 gr. (to free from spasticity).
  - Distilled water: 10 cm.
6. Placement of the electrical apparatus: The body electrodes, covered with rubber, are placed upon the reflex areas (ventral region of Haed and paravertebral region of Abram); the vaginal electrode is placed on the lateral walls of the vagina. One must immediately start the apparatus, augmenting the intensity with each contraction of the uterus until the needed quantity of electricity is obtained

(about 1 watt). The electricity gives only a sensation of profound vibratory massage without ever provoking pain. The patient anticipates the contractions so that by keeping the foot on the pedal of the modulator, one can have the sinusoidal current with a motor-exciting effect during the contractions and, between the contractions, a weakened current with an antispasmodic and analgesic action. Electrical modulation can be obtained even in the absence of the obstetrician (who might be occupied otherwise nearby), thanks to a handle maneuvered by the patient herself, constituting a principle of self-induction.

7. During the entire delivery, the customary rules of obstetrical practice may be carried out and should be observed (rigorous asepsis, complete freedom of the physician's hands permitting obstetrical maneuvers, easy control of the apparatus).

8. At the moment of vulvar expulsion, one can, after having withdrawn the vaginal electrode, regulate the apparatus so that passage of the fetus is accomplished without excessive rapidity.

9. The author usually puts aside the apparatus during the delivery which effects itself very rapidly, but if delivery is delayed, one can provoke the uterine contractions with the aid of the electric current.

10. After the delivery, uterine involution is particularly rapid, but it must be remembered that others have made use of electrotherapy in cases of hemorrhage with uterine subinvolution; also, by continuing the electricity during the days following delivery, the author permits early ambulation, thanks to the advantage of a considerable uterine involution.

The clinical results in a series of over 100 deliveries are presented. The average duration of electrical application in multiparas was 45 minutes with application made at a dilatation of 1 or 2 francs. The average time in primiparas was 1½ hours, application being made with a dilatation of 5 francs. The shortest time was 10 minutes and the longest one hour and 55 minutes. Severe pain attended 10 per cent of the cases, moderate pain, 50 per cent, slight pain, 30 per cent and no pain, 10 per cent. Thirteen deliveries had to be terminated operatively; that is, 6 absolute failures (high forceps and cesarean section), generally for dystocia; 7 relative failures (vulvar forceps). Accidents and incidents are listed as follows:

Maternal: deaths: 0,  
hemorrhages: 0,  
some vomiting: 8 per cent.

Infant: deaths: 1, not attributable to the electrical procedure,  
resuscitations: 3, after deliveries terminated operatively.

In conclusion, the author wishes to insist upon the necessity of using an absolutely correct electro-obstetrical technique in order to obtain valid results. The electrical delivery is harmless and can render real services in certain cases.

A discussion is presented by Chomé, Lantuéjoul and Portes.

Chomé.—First results with the electrical method were astounding enough, since this author succeeded in bringing a primipara of 2 francs dilatation to complete dilatation in 45 minutes with a minimum of pain. A similar result

followed in a 2nd patient. However, then came certain draw-backs. These were edema of the cervix and general accidents to the infants. It was then pointed out to this author by Benoit that the apparatus was badly regulated and investigations were subsequently resumed with the following resultant conclusions:

*Effect of the sinusoidal current at 50 degrees on uterine contraction:* The author has never succeeded with women at term, and not in labor, in provoking regular uterine contractions. He has not observed an intensification of contractions nor an acceleration in dilatation when the current was applied before the dilatation had reached 2 franks in multiparas or 5 franks in primiparas.

*Effect of the current on dilatation:* The author is of the opinion that the current, applied alone without preparatory injection, does not accelerate dilatation in primiparas. In women having received a preparatory injection of pituitary and pantopon, and then the current, the dilatation is accelerated. In this 2nd series, as in the first, several instances have been noted of edema of the cervix with subsequent grave dystocia in certain of the cases.

*Effect of the current on pain phenomena:* It is interesting that certain of the patients claimed a diminution of their pains at the moment of passage of the current.

*Effect of the current on the infant:* If there have been accidents in the infants, these have been due to cervical dystocia.

In conclusion, this author states that the method of Benoit, interesting as it is, requires new investigations and cannot actually be considered as a harmless method of effecting rapid, painless delivery

Lantuéjoul.—One does not speak of the electrical delivery as rapid, painless and without danger. On the other hand, the electric current can have effects on the uterine muscle which are worth studying.

Portes.—It appears that there are 2 points of view in considering this important question. In the first place, the danger of this method is not established. It appears, from the observations of Chomé, that it is distinctly dangerous, particularly in regard to the life of a certain number of infants. It seems that these serious inconveniences should be called to the attention of Benoit. On the other hand, electrical excitation of the uterine muscle produces a certain effect which should be subjected to active research.

(See Editorial Note following next abstract.—Ed.)

## THE OCYTOCIC VALUE OF THE RHYTHMICAL GALVANIC CURRENT

HAMM AND GREIB-HAMM

Gynéc. et obst., 44: 208-10, 1945

The galvanic current formerly employed by the authors necessitated the introduction of the cathode into the cervical canal. It produced rhythmic shocks in

the abdominal wall. To avoid the inconveniences involved in such an occurrence, the writers now use the progressive currents of Lopicque with external electrodes. They have thus treated 19 women.

From a study of these 19 cases, the authors conclude that the repeated application of the progressive galvanic Lopicque current appears to be without danger. A study of its action merits further investigations. Electricity may then be used, in certain cases,—for example, to take the place of posterior pituitary.

Notwithstanding, it is unlikely that the new method will be introduced into general practice, as long as it has not succeeded in shortening labors with a more appropriate current. It is necessary to find the mode of current most congenial with the "current of uterine action", that is, with the nerves effecting uterine contractions.

It is permissible to hope that a new physiological experiment, based on the study of the *chronaxie* of Lopicque will eventually give the necessary indications as to the choice of the best current. Then only, can the method be employed profitably in obstetrics.

(The French have long been interested in hastening labor. Thus, many of us will recall the method proposed by Delmas, about 1930, in which, under spinal anesthesia to relax the cervix, manual dilatation of that organ was carried out from a state of no dilatation at all to complete dilatation in some 30 minutes! And now, in the first French journal to reach us after the war, appears this new method of "electric labor",—another procedure designed to accelerate parturition in normal cases.

Fortunately, the authors as well as the discussants agree that the procedure has no merit in its present status and is not without danger; hence, there is little likelihood of its gaining widespread use even in France. However, as Portes as well as Lantuéjoul point out in their discussions, further research on the effects of electrical currents on uterine contractibility might yield results of practical importance. For instance, what would be the effect of a suitable stimulating current to the uterus in postpartal hemorrhage due to uterine atony?—Ed.)

## A NEEDLE SHIELD FOR CONTINUOUS SPINAL ANESTHESIA DURING LABOR AND DELIVERY

SYLVAN M. SHANE

Am. J. Obst. & Gynec., 51: 283-84, 1946

The author describes the use of a simply constructed needle shield for continuous spinal anesthesia in obstetrics and general surgery. The shield measures 9 inches in length and  $3\frac{1}{2}$  inches in width at the base. The flange, which lies against the back, is lined with felt. The shield is curved in its entirety and is designed for use with a malleable spinal needle.

After insertion of the needle and attachment of regular spinal tubing with a Luer-Lok connection, the needle is bent at right angles  $\frac{1}{4}$  to  $\frac{1}{2}$  inch away from the back and secured with adhesive tape. The needle shield is then placed over the

needle and part of the tubing and secured firmly to the back by placing adhesive tape along the undersurface of the felt-lined flange. This permits the patient freedom to turn on her back or side without the imminence of dislodging the needle or shield.

Since the shield fits comfortably into the lumbosacral curve, it may offer some degree of support to this area when it is anesthetized, possibly helping to minimize postoperative backache. The author concludes that the needle shield makes continuous spinal anesthesia for labor and delivery practicable for the first time. 2 figures.

### EXPERIENCE WITH RECTAL "PENTOTHAL" SODIUM IN OBSTETRICS

GERHART R. TONN

South M. J., 39: 154-58, 1946

The author has employed "pentothal" sodium, one gram per 50 pounds of body weight, in a carefully worked out series of 100 deliveries and reports favorable results.

It was found that the drug is easily given and a nursing staff can easily be trained in its use. The patient was usually more quiet and less apprehensive with "pentothal" than with the other barbiturates and repeated dosage did not increase body movements or stimulate the patient to restlessness. The time of the first stage of labor was decreased in comparison with other barbiturates or without any anesthesia. Much less inhalation anesthesia was needed and induction with ether or nitrous oxide was smooth and simple. The patient responded more rapidly to anesthesia before and during perineal repair. The patient usually reached full consciousness in from 30 minutes to 2 hours with no stupor, headache or typical hangover feeling. The child was nearly always pink and little respiratory difficulty was encountered. No ill effects on the baby could be traced to the carefully administered, thoughtful use of "pentothal". Total amnesia was the rule and rarely did the patient remember anything from the time shortly after administration until after arriving in her room.

Extensive dosage did not stimulate the patient as is frequently seen with the use of other barbiturates and "pentothal" appeared to offer a greater margin of safety to both mother and child. The author found no tendency to hemorrhage or relaxation of the uterus and there was no tendency toward placental retention. The physiological make-up of the patient was very little changed by the rectal administration of "pentothal" sodium. Multipara stated that the drug was far superior to the drugs used in previous deliveries. Oxygen, metrazol and picrotoxin are considered excellent antidotes in case of difficulty.

The author feels that "pentothal" is the least dangerous of all the barbiturates in normal labor, but there are certain definite contraindications for its use. It

should not be administered until the cervix is dilated from 2 to 3 cm. in multiparas and from 3 to 4 cm. in primiparas. Patients who use either alcohol or barbiturates in excess seldom have good results with the use of "pentothal". Primiparas should be selected carefully before administration and the primipara with malposition should be considered a risk with this drug. In conditions of respiratory embarrassment and severe anemia, "pentothal" should not be used. "Pentothal" sodium should not be used with "nembutal", "seconal", "sigmodol" or paraldehyde for best results. It must be used intelligently and on selected patients.

## THE PREVENTION OF PREMATURE LABOR

WALLACE SHUTE AND EVAN SHUTE

J. Obst. & Gynaec. Brit. Emp., 52: 570-74, 1945

The authors present a series of 63 cases of threatened premature labor. Of these, 73 per cent were salvaged. The only therapy used was vitamin E, with or without temporary rest in bed.

In this study it was found that a tendency to premature labor could usually be predicted by finding a blood-estrogen excess even in early pregnancy. Of the patients in this group on whom a blood-estrogen was done, 87 per cent showed a high blood-estrogen. The institution of vitamin E therapy appears to have allowed many cases, otherwise precarious, to carry through to term. However, only a large daily dose of 75 to 125 mg. of Alphatocopherol can save the situation at times. There must be vigorous and adequate treatment with a potent vitamin E preparation until term. As pregnancy progresses the enlarging placenta requires a gradually increasing amount of vitamin E to maintain its "cling" to the uterus.

Of the 109 patients included in this and a previous report, there were 6 monsters delivered, only one, with a cleft palate, surviving over 3 months. However, 92 normal living children were obtained. Their preservation would seem justifiable.

## EARLY CONTROLLED AMBULATION IN THE PUERPERIUM

WM. F. GUERRIERS

Am. J. Obst. & Gynec., 51: 210-12, 1946

It is the purpose of this paper to record the gross data of a large group of patients under controlled ambulation and a detailed report of a smaller group of private patients to show that the advantages of controlled ambulation may be obtained without incurring any of the disadvantages in the puerperal woman.

In 1940, a system of early discharge of the puerperal patient from the 3rd to 5th day under controlled ambulation was instituted. The initial survey of 2926 of these patients revealed the fact that only 30 developed immediate puerperal complications. Postpartum examination of these patients at 6 weeks revealed that the general recovery rate was better in comparison to those cases which remained nonambulatory in the hospital. Relaxations and/or uterine prolapse, malpositions of the uterus and subinvolution of the uterus were present in a smaller number than in nonambulatory cases.

A further detailed study of 323 private patients was undertaken in order to assay the advantages or disadvantages in a class of patients usually seen in private practice. The criterion for allowing ambulation was that patients were medically in a condition to be allowed this privilege.

The method of ambulation is as follows. Every 8 hours for the first 24 hours following delivery, the patient sits on the side of the bed for a few minutes. She sits upright upon the bedpan at each voiding. On the 2nd day the patient stands upright on 4 different occasions followed by sitting upright in a chair for a period of 15 to 20 minutes. On the 3rd day ambulation about the room for short periods of time on 3 or 4 occasions is permitted and complete bathroom privileges are granted. Thereafter, controlled ambulation is permitted with the restriction that each hour of ambulation be followed by an hour of bed rest. By the 10th day the patient is completely ambulatory and at the end of the 21st day she is allowed to resume complete outdoor ambulation without unduly tiring herself.

There were 227 primigravida cases and 96 multigravida in this series. There were 318 vertex and 5 breech presentations. Outlet forceps were employed in 285 instances, midforceps in 7, Piper forceps in 5, and manual aid in 2. Caudal analgesia was used in 103 cases, local pudendal block in 30 and gas anesthesia in 190 cases. Episiotomies were performed in 290 cases.

In all instances the patients expressed that a general feeling of well-being occurred from the ambulation. Lochia drainage was greatest in the first 3 to 5 days with a rapid decrease until almost complete cessation by the 10th day. Catheterization was not necessary in a single instance and bowel function was normal without the use of enemas or cathartics. In all but 6 instances uterine involution was accelerated, the uterus being in the pelvis by the 10th day. Complete healing of episiotomies was present by the 7th day in all but 2 cases. In 10 cases morbidity was present for an average of 3 days; these included 2 cases of pyelonephritis, 3 of endometritis and 5 of mastitis. There was present no immediate severe postpartum bleeding. At 6 weeks there was subinvolution in 4 cases and retroposition of the uterus in 16 cases. At 6 months there was an absence of any additional abnormality as compared with the 6 weeks examination. Particular reference to the possibility of relaxation and/or prolapse revealed nothing of note.

It is concluded that early controlled ambulation offers advantages to the obstetrical patient without imposing any disadvantages.

should not be administered until the cervix is dilated from 2 to 3 cm. in multiparas and from 3 to 4 cm. in primiparas. Patients who use either alcohol or barbiturates in excess seldom have good results with the use of "pentothal". Primiparas should be selected carefully before administration and the primipara with malposition should be considered a risk with this drug. In conditions of respiratory embarrassment and severe anemia, "pentothal" should not be used. "Pentothal" sodium should not be used with "nembutal", "seconal", "sigmodol" or paraldehyde for best results. It must be used intelligently and on selected patients.

## THE PREVENTION OF PREMATURE LABOR

WALLACE SHUTE AND EVAN SHUTE

J. Obst. & Gynaec. Brit. Emp., 52: 570-74, 1945

The authors present a series of 63 cases of threatened premature labor. Of these, 73 per cent were salvaged. The only therapy used was vitamin E, with or without temporary rest in bed.

In this study it was found that a tendency to premature labor could usually be predicted by finding a blood-estrogen excess even in early pregnancy. Of the patients in this group on whom a blood-estrogen was done, 87 per cent showed a high blood-estrogen. The institution of vitamin E therapy appears to have allowed many cases, otherwise precarious, to carry through to term. However, only a large daily dose of 75 to 125 mg. of Alphatocopherol can save the situation at times. There must be vigorous and adequate treatment with a potent vitamin E preparation until term. As pregnancy progresses the enlarging placenta requires a gradually increasing amount of vitamin E to maintain its "cling" to the uterus.

Of the 109 patients included in this and a previous report, there were 6 monsters delivered, only one, with a cleft palate, surviving over 3 months. However, 92 normal living children were obtained. Their preservation would seem justifiable.

## EARLY CONTROLLED AMBULATION IN THE PUERPERIUM

WM. F. GUERRIERS

Am. J. Obst. & Gynec., 51: 210-12, 1946

It is the purpose of this paper to record the gross data of a large group of patients under controlled ambulation and a detailed report of a smaller group of private patients to show that the advantages of controlled ambulation may be obtained without incurring any of the disadvantages in the puerperal woman.

It is evident from the study that as parity increased there was a rise in the percentage of abortions. Four hundred and eighty patients in the series were pregnant for the first time and of those 49 aborted spontaneously. However, as only 10.2 per cent of the primigravidas aborted spontaneously as compared with 9.4 per cent of the whole series, this group does not seem numerically important.

In addition to the 108 abortions, there were 66 threatened abortions in which some vaginal bleeding was present, with or without cramps some time during the pregnancy, the majority occurring in the first trimester. Those admitted to the hospital were treated with bed rest and progesterone orally. There were 2 patients with early rupture of the membranes. They had some abdominal pain but no bleeding, and both went on nearly to term and were delivered of living children. If these 68 cases are added to the 94 who aborted spontaneously, it makes a total of 162, or 43 per cent of successfully treated cases of threatened abortion. However, 3 patients who were treated successfully had deformed babies (1 microcephalus and 2 spina bifidas).

The average age of the aborters was 31.8 years, the extremes being 18 and 43 years. The average age of those who did not abort was 27.07, the extremes being 13 and 44 years. Falls and intercurrent infections were of no etiologic consequence in the series. Pelvic inflammatory disease was encountered only 3 times, but 2 of these cases aborted. One of 4 patients with uterine fibroids aborted.

Patients who were overweight and those with low basal metabolic rates seemed prone to abort; 94 of the 1,000 weighed more than was proper for their age and height. Two of these were in the therapeutic abortion group and 11 in the spontaneous abortion group. Eighty-one overweight women went to term. Only one patient in the entire series suffered from underweight and she was one of 2 with hepatitis who were aborted.

The history of a previous sterile period would seem of significance. Nine patients with such a history aborted spontaneously and 21 went to term. Further evidence of defective germ plasm is seen in the number of deformities in the infants. One baby had clubbed feet and one polydactylism; 2 had cleft palate. One infant had atresia of the small intestine, confirmed at autopsy. There was one iniencephalus and one microcephalus. Two babies had spina bifida and 2 had hydrocephalus. An additional one had a combination of spina bifida and hydrocephalus. As noted before, the microcephalus and 2 of the spina bifida infants were born to mothers who had threatened to abort.

Among the gynecologic conditions associated with the 1,000 pregnancies were 23 cases of vaginitis severe enough to warrant treatment. One of these women aborted spontaneously and 22 went to term. As mentioned before, there were 3 cases of pelvic inflammatory disease, one aborting spontaneously and one 3 weeks following a fall; the third went to term. Four uterine myomas were noted; 3 of these went to term, the fourth having a spontaneous abortion. Retroversion of the uterus is probably an important etiologic factor; 44.1 per cent of the patients who aborted had this condition on postpartum examination, as compared with 26.9 per cent of those who had term deliveries.

## **PATHOLOGY OF PREGNANCY**

### **SPONTANEOUS ABORTION**

**GWEN S. HUDSON AND M. PIERCE RUCKER**

**J. A. M. A., 129: 542-44, 1945**

The authors state that for several years it had seemed to them they were having more abortions than they should in their patients. They realized that patients are now consulting obstetricians earlier in pregnancy than formerly. Some few years ago many patients who aborted early had not even consulted a doctor. Probably the apparent increase in the rate of abortions may not be real, but the problem is a real one, especially for the previously sterile patient.

The abortion rate is difficult to determine, being variously estimated. One authority estimated that from 600,000 to 700,000 abortions occurred in the United States each year, calculating one abortion for every 2.5 confinements in urban areas and one for every 5 confinements in rural districts. It is thought that one abortion to every 6 confinements is more nearly correct. Other writers found a fairly constant proportion of abortions and stillbirths in various hospitals and clinic studies of 2.6 per cent stillbirths and 12.1 per cent abortions. Anatomists and embryologists have reported a surprisingly high percentage of defective ova in early conceptuses. In 17 human embryos obtained before the mother had time to miss a period, 2 investigators noted that 5 were so defective that they could not have developed; which meant that 42 per cent of the embryos were defective at the very beginning.

The authors of this article studied the histories of 1,000 pregnancies whose termination was under their care. Some of the pregnancies, chiefly consultation cases, came under their observation only at the end of the pregnancy. An ideal group of cases for such a study would be composed of those which had been under observation from the premarital examination until they had passed the child-bearing period, but the authors know of no such study. They checked the histories of 250 married patients who had passed the menopause. These women had 596 children and 182 abortions. This is an average of 2.38 children and 0.73 abortions per mother; one abortion in every 4.28 pregnancies.

In the 1,000 consecutive cases studied from June, 1943 to May 8, 1945, there were 107 abortions. One patient died undelivered, of a gas bacillus infection following an attempted criminal abortion. This was the only maternal death in the series. There was one other criminal abortion in the group; she also had a gas bacillus infection, but recovered. There were 12 therapeutic and 94 spontaneous abortions. Five therapeutic abortions were done for hypertension; 2 were done for hepatitis; one on account of tuberculosis; one for heart disease; one was a mental case; one had otosclerosis; one had diabetes and was not doing well.

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## ECTOPIC PREGNANCY

H. H. WARE, JR. AND W. C. WINN

South M. J., 39: 44-49, 1946

Ectopic pregnancy is an important cause of maternal deaths. The authors observe that, during specified periods of time, ectopic pregnancy was the cause of maternal death in every 16th case in New York City, in every 12th case in Chicago, in every 18th case in Philadelphia and in every 11th case in Richmond. It has been observed once in every 300 pregnancies by one source and once in every 403 pregnancies by another.

The treatment of ectopic pregnancy is fairly well standardized; it is in diagnosis that failures occur. In the present paper, the authors report 115 cases treated during the last 5 years and review the important points in diagnosis. In this series, two-thirds of the patients were between the ages of 20 and 30 years and 84 per cent were between the ages of 20 and 35 years. Thirty per cent were white and 69 per cent were Negro.

Ectopic pregnancy should be suspected in any woman in the child-bearing age who has abdominal pain, particularly if it is located in the pelvis and unilateral in type. This pain, in cases of ectopic gestation, is frequently described as sharp, lancinating, stabbing or tearing, but sometimes cramplike and usually intermittent even though dull. The pain usually has a definite onset and is frequently noticed after exertion, defecation, and sometimes after intercourse. The severity of shock is in proportion to the rapidity of onset as well as to the amount of internal hemorrhage. A careful history reveals an irregularity of the menses, either in interval or amount and duration of flow. Amenorrhea for one month or more is frequent. The presence of a unilateral, exquisitely tender, boggy mass in the pelvis increases the probability of this accident. The presence of such a mass was diagnosed in 51 per cent of the patients in this series. Manipulation or pressure on the cervix causes severe pain in most cases.

With the possibility of an extra-uterine pregnancy in mind, one should analyze history and symptoms to decide whether the patient has an acute rupture of the tube or pregnancy, or a leaking or previously ruptured ectopic which has become walled off and developed as an abnormal pelvic mass. The first condition has the indications for immediate operation; in the second condition one should rule out pelvic inflammatory disease and small pelvic tumors before operating. Of the 115 cases in this series, 67 per cent were admitted with an acute rupture of the pregnancy and 32 per cent were admitted with a pelvic mass. Sharp lancinating or cutting pelvic pain with fainting was recorded 10 times more often in acutely ruptured cases than in cases with pelvic mass. Pelvic pain of dull aching character was recorded 3 times more frequently in patients with a pelvic mass than in those with acute rupture. Shoulder pain was 8 times more frequent in the acutely ruptured patients. Slight vaginal bleeding or spotting was recorded twice as often in patients with pelvic mass. Seventy-eight per cent of the present series

had some vaginal bleeding but in none was it profuse. This is an important point in differentiating from incomplete abortion. The only patient who passed large clots also had multiple uterine fibroids. The incidence of acute rupture was the same in those patients having no amenorrhea as in those who had missed one or more menses.

A rapid pulse rate is one of the most characteristic findings in ruptured ectopic gestation. The pulse rate was above 90 in 2 out of every 3 cases in this series. The blood pressure is usually normal in patients with a pelvic mass and below 100 systolic most frequently in the acutely ruptured cases. The temperature is usually normal or slightly elevated; the combination of rapid pulse and slight elevation of temperature is considered a valuable aid in ruling out pelvic inflammatory disease. The white cell count increases immediately after rupture of an ectopic but usually drops to normal within 24 hours unless there is a recurrence of the bleeding. The red cell count is low most frequently in acutely ruptured cases. Low hemoglobin is suggestive of ruptured ectopic gestation.

The incidence of mortality in these 115 cases was 1.7 per cent. In an earlier series of 150 cases it was 8 per cent. The authors believe that early operation was partially responsible for this reduction.

## ECTOPIC GESTATION; THE DIAGNOSTIC VALUE OF CUL-DE-SAC ASPIRATION

L. E. BURCH AND J. SEITCHIK

*Am. J. Obst. & Gynec.*, 50: 765-70, 1945

Extrauterine pregnancy is more often overlooked, and more often diagnosed when not present, than any other serious pelvic lesion. The authors have divided ectopic gestation into 2 varieties; the typical, comprising 40 per cent of the cases, and the atypical, comprising 60 per cent. In the typical case, a quick diagnosis and early operation is urged. In the atypical variety, the patient is not in shock, the sighing respiration and blanched appearance are absent and the thready pulse and subnormal temperature are not present. It is in this variety that time can be taken to make use of procedures so useful in arriving at a correct diagnosis.

The authors have found the injection of carbon dioxide gas into the peritoneum through an abdominal puncture followed by an x-ray of the pelvis a procedure of great diagnostic value. It is free of danger but can be used only in those institutions where there is close cooperation with the x-ray department.

Particular emphasis is placed, in this paper, upon the value of aspiration of the peritoneum either per vaginam or through the abdominal wall if conditions in the cul-de-sac make it not advisable to aspirate per vaginam. If the aspirated blood shows an absence of rouleaux formation and the erythrocytes show a crenated appearance, it signifies a hemorrhage into the peritoneal cavity. In

obtaining blood from the peritoneal cavity, color, viscosity, presence of small clots and clotting time are noted. The old blood has a definite brownish tint, is thinner than fresh blood and does not clot.

The authors consider aspiration the most valuable of all aids in making a diagnosis of doubtful cases of ectopic gestation. They are of the opinion that with a careful study of this most interesting and sometimes fatal condition, giving due consideration to the history, the physical signs, the laboratory tests, x-ray and especially aspiration, the margin of error will be greatly reduced.

(In this statistical study of 105 patients, the authors emphasize particularly the diagnostic value of aspiration per vaginam or through the abdominal wall. It is probably true that most clinicians do not employ this as frequently as the authors, but its value would seem to be attested by the fact that in 21 of their cases in which operation was done after cul-de-sac puncture, not a single error in diagnosis was revealed.—Ed.)

## APLASTIC ANEMIA SIMULATING ECTOPIC GESTATION; REPORT OF A CASE

S. KOLODNY AND S. T. DeLEE

*Am. J. Obst. & Gynec.*, 51: 130-31, 1946

The etiology of aplastic anemia is unknown; however, an unidentified toxin is believed to act upon bone marrow, impeding its activity and causing atrophy. The author reports a case of aplastic anemia which simulated ectopic gestation.

The patient, a 29-year-old woman, was admitted to the hospital complaining of weakness, dizziness, fainting and severe epigastric pain. Her last menstrual period had occurred 11 days previously and was very profuse. Her occupation was that of a factory radio worker, in which she ground quartz crystals using carbon tetrachloride. In the last 10 days her gums had bled easily. Physical examination revealed a very anemic patient who appeared acutely ill. A soft systolic apical murmur was heard. On her back, were several small areas of ecchymosis. There was tenderness in both lower quadrants and on pelvic examination, in both adnexal areas. The cervix and uterus were normal. The impression was ruptured ectopic pregnancy; a blood dyscrasia was considered.

A laparotomy was done which revealed the pelvis full of fresh dark blood; the uterus, tubes and ovaries were normal except for bleeding from the ostium of the left tube. A left salpingectomy was performed. Following surgery and transfusion, the patient's condition improved for 3 days. On the 4th day she became somewhat icteric and developed petechiae of the forearms, gums and conjunctivae. At this time the erythrocytes were 2,240,000, leucocytes 2200, hemoglobin 23 per cent, platelets 125,000, icteric index 40, cevitic acid level 35, nonprotein nitrogen 29, uric acid 3, and chlorides 580. A sternal puncture gave the following findings; Marrow for the most part fibrotic with an incomplete disappearance of normal cellular elements. Throughout the marrow were found

occasional groups of what appeared to be diplococci. The opinion was that the material represented an aplastic marrow with secondary lymphoid degeneration as evidenced by maturity of the cells seen. A diagnosis of aplastic anemia was made.

In spite of treatment, on the 19th postoperative day, the temperature went to 106 degrees F. and the patient expired.

## SELECTIVE TREATMENT OF ANTEPARTUM HEMORRHAGE

W. A. Scott

Am. J. Obst. & Gynec., 51: 48-56, 1946

The author presents the results of selective treatment of 191 cases of placenta previa with a mortality of 2.6 per cent; and 139 cases of accidental hemorrhage with a mortality of 2.9 per cent. These results are believed to be comparable to those obtained by routine section in the treatment of these conditions and may avoid the additional risk of subsequent pregnancies by patients who have undergone cesarean section.

It is worthy of note that in the 911 cases of placenta previa, 3 patients had spontaneous deliveries without maternal death or severe blood loss in spite of the fact that the placenta completely covered the internal os at the time of examination. An analysis of the maternal mortality in this series of 191 cases shows that of the 5 deaths, one followed cesarean section, one occurred 20 minutes after admission in an undelivered patient and 3 followed version. It is noted that expectant treatment and cesarean section have by far the lowest fetal death rate. It has thus been shown that treatment of placenta previa becomes a matter of judgment and that the factors which influence choice of method are: situation of placenta, amount of bleeding, parous condition of patient, whether or not labor has begun and how it is progressing, duration of pregnancy, presentation of fetus and whether or not the fetus is viable.

In the series of 139 cases of accidental hemorrhage there were 4 deaths. One of these was due to anuria following conservative treatment, one to sepsis following the introduction of a bag, one to cardiac failure after classical cesarean section and the 4th died undelivered. In this series only 11 were treated by section. The incidence of fetal mortality in the 11 cases of cesarean section was 81 per cent. In the 128 cases treated by other methods the incidence was 57 per cent.

The author concludes that all cases of antepartum hemorrhage should be treated in the hospital if at all possible, and as the diagnosis cannot always be made accurately when the first bleeding is only slight, this will entail hospitalizing patients who may subsequently be proved to have neither placenta previa nor accidental hemorrhage.

In most emergencies of medical practice, where special skill is not available,

conservative measures of treatment are usually in the best interest of the patient, but in placenta previa and probably in accidental hemorrhage, if skilled judgment is not available, radical method of treatment, namely cesarean section, is probably advisable.

## THE MANAGEMENT OF PLACENTA PREVIA

LUIS GUTIERREZ YEPES AND N. J. EASTMAN

South. M. J., 39: 291-97, 1946

The purpose of this paper is to review the results obtained in 304 cases of placenta previa seen at the Johns Hopkins Hospital over the past half century in

TABLE IV

*Maternal, stillbirth and neonatal mortality rates during the three periods studied*

	PERIOD I 1896-1919	PERIOD II 1920-1934	PERIOD III 1935-1944
<b>Treatment</b>			
Total cases .....	65	128	111
Cesarean sections .....	2 (3.1%)	9 (7.0%)	64 (57.7%)
Patients transfused .....	2 (3.1%)	19 (14.8%)	51 (45.9%)
<b>Results</b>			
Maternal deaths .....	9 (13.8%)	10 (7.8%)	1* (0.9%)
Stillbirths .....	41 (63.1%)	61 (47.7%)	26 (23.4%)
Neonatal deaths .....	10 (15.4%)	24 (18.7%)	26 (23.4%)
Total infant loss .....	51 (78.5%)	85 (66.4%)	52 (46.8%)

\* Death due to rupture of uterus following Braxton-Hicks version.

the hope of eliciting some conclusions about the advantages and dangers of the various methods which have been recommended for the management of this condition.

The entire time interval covered by this study has been divided into periods according to the dominating policies of management pursued. During period I (1896-1919), vaginal delivery without blood transfusion was the usual treatment; during Period II (1920-1934), vaginal delivery, for the most part, with a moderate number of blood transfusions was employed; during Period III (1935-1944), cesarean section supplemented by the liberal use of transfusion was employed in the majority of cases.

The statistics shown in Table IV are convincing evidence of the life-saving value of cesarean section in placenta previa. The infant mortality rates in this series are also noteworthy as it is shown that the reduction in infant mortality in Period III, when compared with Period I, was 40 per cent. Although cesarean section for the sake of the baby can never be advanced as a valid argument for

the general use of abdominal delivery in placenta previa, it does promise an appreciably better outlook even for the premature infant and a decidedly better prognosis for the mature child.

It is the authors' opinion that blood transfusion shares equally with cesarean section the credit for the low maternal mortality rate during Period III.

The authors' experience has been similar to that of others in that central and partial placenta previa show, when treated vaginally, a very high maternal mortality, whereas marginal placenta previa, however handled, is attended by a much lower death rate.

Thirteen of the 20 maternal deaths were due to exsanguination; in 8 of these postpartum blood loss played a decisive role. In the 11 autopsies performed, 6 revealed either actual rupture of the lower uterine segment or extensive cervical lacerations.

Both the friability and the vascularity of the cervix and lower uterine segment increase with the completeness of the placenta previa. Consequently, the employment of the bag or Braxton-Hicks version will result in lacerations in a certain proportion of cases, particularly in the central and partial types. Herein lies the basic rationale for the employment of cesarean section in placenta previa, and the authors feel (in so far as it is possible to generalize) that abdominal delivery should be employed in all cases of this complication with the exception of marginal types in multiparae with vertex presentations. In the latter cases, gentle rupture of the membranes supplemented if necessary by the Willett forceps, will usually suffice.

## HYDATIDIFORM DEGENERATION OF PLACENTA, COMPLETE WITH FETUS

ABE CLINE

*Am. J. Obst. & Gynec.*, 51: 132-33, 1946

The case is presented of a woman, 18 years of age, who was admitted to the hospital complaining of cramps and vaginal bleeding. Her last normal menstruation had been 5 months previously. Ergotrate, 1/320 grain, was ordered 3 times a day and later, on examination, a dark red firm clotlike mass presented just within the vulvular orifice. It was removed with a sponge forceps. Grossly, the mass appeared to be placental tissue. The pathologist reported finding hydatid vesicles, whereupon a curettage was performed. A moderate amount of endometrium and clots were obtained. More careful examination of the original specimen showed that it included a small papyraceous fetus within a sac, attached by an umbilical cord to a placenta which had undergone partial hydatidiform degeneration. The specimen was of interest because it showed a fetus of 6 to 8 weeks' size with a placenta of about 16 weeks' size. The pathological diagnosis was: (1) hydatidiform mole; (2) degenerated fetus, 6 to 8 weeks. 1 figure.

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ents. In the course of the investigations it was seen that diets very low in sodium content appeared to exert a hypotensive effect, which was abolished by the addition of sodium chloride. The association of a low sodium content of the diet with a hypotensive response was so striking that the studies were extended to a series of patients. The results thus far obtained would appear to indicate that in certain patients this form of therapy is decidedly beneficial. The present paper is confined to the observations on human beings only.

Six subjects were investigated while rigidly controlled in the hospital. The blood pressure was taken twice daily, at least five readings being made each time, and the results averaged.

The diets used were made up of foods naturally low in sodium content. In order to provide an adequate protein intake and at the same time achieve drastic sodium restriction, it was necessary to dialyze the milk consumed by the patients. In this way it was possible to administer a 2,000 calory diet daily which contained less than 1 Gm. of sodium chloride.

In two of the six patients, the blood pressure declined to essentially normal levels and promptly rose again to the pretreatment values when 20 Gm. of sodium chloride was added daily to the diet which had previously resulted in a reduction of their blood pressure. Subsequent cessation of the use of the added sodium chloride again resulted in a decline in blood pressure. In one patient there was no decline in blood pressure and in the remaining 3 there resulted a moderate reduction. However, one of these 3 patients displayed acute circulatory collapse which responded promptly to sodium chloride therapy. The authors present case abstracts of this series which give more detailed information concerning the patients and results.

The use of a "low salt" diet in the therapeutic management of patients with hypertension has been advocated by observers in this country, in France and Germany, who apparently believed that any beneficial effects were due mainly to chloride restriction, and did not seem to appreciate the peculiar significance of the sodium ion. However, the definitive value of drastic salt restriction has not been accepted generally, and this form of therapy has never been widely used. Moderate restriction of sodium usually fails to influence appreciably the blood pressure, and the employment of moderate, rather than drastic restriction is probably the reason this form of therapy has not been successful. The lack of controlled observations on animals with experimental hypertension militated against the acceptance of this procedure.

From a practical point of view it may be necessary that salt restriction be extremely rigid if it is to be effective. This is best accomplished by dialyzing such food as milk, to remove the sodium chloride, selecting foods naturally low in sodium content and by the liberal use of flavoring agents to overcome the insipid taste of salt-free food. It is also necessary to observe the patients closely, particularly in hot weather, for symptoms of salt deprivation. In view of the relative ease with which this method can be applied, it seems to offer, for certain patients, the most practical and effective therapeutic measure that is at present available. It is suggested that the diet be utilized for a brief trial period for

(One is apt to forget that hydatidiform molar changes may affect only small localized portions of the placenta, and that such partial hydatidiform degeneration need not interfere with the nutrition of the fetus. A considerable number of cases have been reported in which full term delivery of normal living babies has occurred under such circumstances.—Ed.

## PYRIDOXINE FAILURE IN NAUSEA AND VOMITING OF PREGNANCY

H. CLOSE HESSELTINE

Am. J. Obst. & Gynec., 51: 82-86, 1946

Until factual evidence can be produced, it is proposed that pyridoxine in the dosages and methods used is of no more value in treatment of mild or moderate nausea and vomiting of pregnancy than scores of other preparations.

In the present series of 16 patients, 11 were given pyridoxine initially; 3 of these had good results, 3 had fair results and 5 had poor results. A control group of 5 patients were initially placed on placebo therapy. Three of these 5 were completely relieved. Two had poor results. Placebo therapy was used in 3 of the pyridoxine-treated group, secondarily. One of these obtained good results on placebo therapy and another had an excellent result on moderate sedation. Only one patient in the entire series was a hyperemesis gravidarum case and she was cured only with the use of sedatives and other measures. Every one of the 16 patients was cured and the pregnancy carried on.

The use of pyridoxine as advocated in the literature for hyperemesis gravidarum is valueless and without justification. This report does not imply that pyridoxine is not an essential vitamin but refers only to its use in the treatment of mild nausea and vomiting of pregnancy as well as hyperemesis gravidarum. These observations reaffirm the need for proper controls in all clinical and therapeutic research. The author advances a serious and earnest plea for critically controlled studies of all procedures and that publication be withheld until such controls are obtained.

## SODIUM RESTRICTION IN THE DIET FOR HYPERTENSION

ARTHUR GROLLMAN, T. R. HARRISON, M. F. MASON, JAMES BAXTER,  
JOSEPH CRAMPTON AND FRANCIS REICHSMAN

J. A. M. A., 129: 533-37, 1945

In connection with the studies of experimental hypertension the effects of various types of diet on the blood pressure have been noted, including alterations in the content of vitamins, proteins, minerals and certain other dietary constitu-

urinalysis, weight, general signs and symptoms being noted and analyzed from time to time. If abnormalities indicative of toxemia develop, the regime must be intensified by rest and dietary restriction. Bed rest is the most important single item of prophylaxis and treatment of milder cases. Estimations of renal capacity, blood chemistry and sometimes hepatic function are made. Liquid intake and urinary output are watched and correlated and bowel function is maintained. Failure of the mild type to improve under such a regime, or its progression, should in a short time lead to the consideration of the termination of pregnancy.

Means employed for this purpose are usually medicinal, it being preferable not to resort to mechanical means. If necessary, cesarean section should be done. Anesthesia is of great importance; no inhalation anesthetic should be used.

In the event of an actual state of eclampsia, the patient is placed in complete quiet and seclusion. Magnesium sulfate (20 cc. of a 10 per cent solution) is administered intravenously at one-hour intervals as long as convulsions persist. An initial dose of morphine sulfate,  $\frac{1}{4}$  grain by hypodermic, may be given. Other sedatives should be used in substitution for, rather than in addition to, those already prescribed. Dextrose solution is given intravenously to reduce the edema and act as a diuretic. Drainage of tracheal mucus is done if necessary. Venesection is used only in right heart failure. Liquids of high carbohydrates equivalent are given as soon as the patient can swallow. This scheme of management does not contemplate termination of pregnancy during the actual period of convulsion and/or coma. However, if the patient recovers from the crisis undelivered and with a viable baby, the authors believe that within a few days the pregnancy should be terminated.

The primary objective of all management is (1) to reduce maternal mortality. Direct secondary objectives contributing to this purpose are (2) prevention of eclamptic convulsions, and (3) prevention of abruption of the placenta. Next to the life hazard of the mother, (4) life hazard to the fetus in abortion, stillbirth and neonatal death becomes the most important consideration of management. Finally, (5) reduction of remote hazard of death to the mother by the prevention of permanent sequelae is a further objective.

## TOXEMIA OF PREGNANCY WITH UNUSUAL POSTMORTEM FINDINGS

FREDERICK WEINTRAUB

*Am. J. Obst. & Gynec.*, 51: 275-77, 1946

Two cases of toxemia of pregnancy resulting in death are presented by the author. The postmortem findings were as follows:

Case 1. Both kidneys were palpated and were felt to be filled with stones. Parenchyma was relatively thin and calculi could be felt to move beneath the

patients with hypertension and employed for a longer time in subjects who display a favorable response.

(This noteworthy study carries obvious implications in regard to the management of the hypertensive toxemias of pregnancy. In the first place, it re-emphasizes the transcendent importance of salt restriction in the management not only of pre-eclampsia but of chronic hypertensive disease in pregnancy. In the second place, it raises the question as to whether we obstetricians have pushed salt restriction as far as we might. The usual diet given in most hospitals to pre-eclamptics is a "salt-poor" diet, no salt being added in cooking nor by the patient. Under such circumstances the natural salt in foods yields a salt intake of 4 or 5 Gr. per day. If we had the milk dialyzed and exercised other precautions, it is apparently possible to reduce sodium chloride intake to about 1 Gr. per day and the question is: might not this help in extreme cases of pre-eclampsia which we are trying to carry nearer term?—Ed.)

## THE MANAGEMENT AND TREATMENT OF THE LATE TOXEMIAS OF PREGNANCY

S. A. COSGROVE AND L. C. CHESLEY

*Am. J. Obst. & Gynec.*, 51: 67-74, 1946

By "toxemia of pregnancy" is understood a disturbance occurring during or in connection with pregnancy, consisting of a variety of syndromes, the most constant factors of which are hypertension, proteinuria and edema. To these might be added a variety of renal, gastrointestinal and nervous symptoms. In an attempt to standardize present concepts of pathologic and symptomatic variations into a system of nomenclature, the American Committee on Maternal Welfare adopted the now familiar system of nomenclature which divides toxemias into 4 groups. Group A represents disease not peculiar to pregnancy, including hypertensive and renal disease. Group B signifies disease dependent on or peculiar to pregnancy, including pre-eclampsia and eclampsia. Group C represents vomiting of pregnancy and Group D unclassified toxemias.

The pathology of the disease is as various as its symptomatology yet there is no absolutely pathognomonic picture. Among the more constant pathologies are those involving the liver, kidneys, brain, vascular system, heart, adrenals, pituitary and organs of special sense, notably the eyes. Ideas of pathogenesis have been closely linked with shifting conceptions of pathology. Even today, the author is unable to add to the statement of Whitridge Williams: "It is apparent that the cause of eclampsia has not yet been discovered."

Lacking then any established knowledge of etiology and pathogenicity, the management and treatment of the late toxemias of pregnancy remain on the same basis as formerly established. Its 3 phases are: (1) prophylaxis; (2) treatment of symptoms; and (3) termination of pregnancy.

The author summarizes briefly the method of treatment. Prophylactic treatment includes the entire regime of antenatal care, with history, blood pressure,

On February 24th she exhibited for the first time a show of blood accompanied by abdominal pain. On the 25th she expelled the contents of the uterus which proved to be an embryonic mole. The toxic symptoms did not reappear and the patient was discharged in 15 days, no longer having albuminuria.

Noteworthy is the abrupt disappearance of the toxic phenomena while the mole continued to develop. The death of the fetus appears to be the only explanation of the disappearance of the toxic phenomena.

### BLOOD-PRESSURE OF RELATIVES OF PATIENTS WITH TOXAEMIA OF LATE PREGNANCY

JOSEPHINE BARNES AND F. J. BROWNE

J. Obst. & Gynaec. Brit. Emp., 52: 559-69, 1945

It is well known that a tendency to high blood-pressure may be inherited though the evidence for this is based on records of individual families rather than on statistical study. Many individual reports have appeared of the occurrence of eclampsia in several members of the same family. A tendency to hypertensive disease in relatives of patients suffering from eclampsia has also been noted.

The authors present a series of 226 relatives of 129 patients who were admitted to the hospital with toxemia of pregnancy. The blood-pressure of the relatives was recorded. The patients have been divided into 4 groups: (1) eclampsia; (2) pre-eclamptic toxemia; (3) essential hypertension and pregnancy; and (4) unclassifiable toxemia. The blood-pressure was also estimated in 66 relatives of 47 control patients who were not suffering from toxemia.

A demonstrable difference in the levels of blood-pressure has not been noted between the relatives of toxemic and control patients, except in cases of essential hypertension and pregnancy. However it was found that 16 among 18 mothers of these patients were markedly hypertensive. It is concluded that there is not any evidence that a hereditary tendency to hypertension is of any general importance in the etiology of toxemia of pregnancy except in cases of essential hypertension and pregnancy.

The authors discuss the implications of these findings and conclude that it is rarely necessary to interrupt pregnancy in a case of essential hypertension in the interests of the mother. Nor should patients with a familial history of hypertensive cardiovascular disease be discouraged from having children, except in those very rare cases in which the manifestations of the disease have occurred frequently and at an early age.

(Since the obstetrical service at the Johns Hopkins Hospital extends back to 1896, many of our mothers were themselves born in this hospital and in some cases their mothers also. The case histories throughout this long period are fairly complete and a few years ago I had a similar notion to that of Barnes and Browne, namely, that it might be possible to dem-

palpating fingers. On section the greater part of the kidney was seen to be occupied by numerous calculi varying in size from a pinpoint to a small grape. There were approximately 1000 stones in each kidney. Stones were found in the pelvis of the kidney and gravel in the upper portion of the ureter. The bladder mucosa showed focal areas of injection but no ulceration. The uterus was the size of a 6 months' gestation. The pathological diagnosis was bilateral obstructive calculous pyonephrosis with uremia associated with pregnancy; splenomegaly and hepatomegaly due to chronic passive congestion; hypostatic congestion of the lungs.

. This case demonstrates the possibility that massive calculous disease of both kidneys may escape clinical recognition. Pregnancy was contraindicated and its continuence undoubtedly hastened the fatal uremic outcome.

Case 2. The liver weighed 1120 grams. Glisson's capsule over the left liver lobe was lifted off the liver parenchyma by a large subcapsular hematoma and at one place the capsule was broken permitting the subcapsular accumulation of blood to ooze into the abdominal cavity. Smaller hematomas were scattered over the liver surface. The picture was dominated by confluent hemorrhages with areas of yellowish necrosis interspersed. The serosal surface of the gall bladder was mottled with hemorrhages. The pathological diagnosis was diffuse hemorrhagic necrotizing hepatitis, as seen in eclampsia gravidarum, massive subcapsular hemorrhage of the liver, gravid uterus with about 6½ month fetus in situ, tubal nephrosis, focal myocarditis (toxic variety).

This case merits a report since profuse intra-abdominal hemorrhage originating in the liver as an immediate cause of death in eclampsia is rare.

## SEVERE ECLAMPSIA IN THE THIRD MONTH OF GESTATION; EMBRYONIC MOLE

RAVINA AND JAMAIN

Gynéc. et obst., 44: 185-86, 1945

The authors describe the case of a 22-year-old primipara who was admitted to the hospital on December 29, 1943 in a profound coma. She appeared to be at about the 3rd month of gestation. During the first 24 hours in the hospital she had a dozen convulsions characteristic of eclampsia. There was massive albuminuria and hematuria. In spite of a grave prognosis at the time of entrance, the patient responded to classical treatment, the eclamptic seizures became less frequent and the temperature became normal. There was no evidence of bleeding and at the end of 15 days the patient was discharged, having only some traces of albumin.

She was followed regularly. The uterus continued to increase in size but the patient could not feel fetal movements and the heart beats were not perceived.

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onstrate a hereditary tendency to pre-eclampsia and eclampsia. However, after reviewing some 400 histories I could find no correlation whatsoever and hence can confirm the above findings.—Ed.)

## ACUTE HYDRAMNIOS; A BRIEF SURVEY OF THE RECENT LITERATURE, WITH REPORT OF A CASE SIMULATING CONCEALED ACCIDENTAL HAEMORRHAGE

D. T. O'DRISCOLL

J. Obst. & Gynaec. Brit. Emp., 52: 496-500, 1945

The rarity of acute hydramnios is illustrated by the fact that there are only 90 cases to date recorded in the literature. The etiology of the condition is still unknown, but the author suggests that pathological conditions, both on the maternal side and on the fetal side (including chorion, amnion and umbilical cord), may be contributory if not sole causes. Analysis of 40 cases of acute hydramnios reported in the literature since 1914 shows that 8 cases were associated with twin pregnancy, 7 cases with anencephalic fetuses and 2 cases with teratoma of the neck. Other fetal anomalies occurring singly were: multiple deformities, atresia of the esophagus, congenital adenoma of the lung and hydrocephalic anophthalmic monster. Maternal associated conditions were: ascariasis (acute puerperal), diabetes mellitus and eclampsia.

The case is presented of a 23-year-old primigravida who attended the antenatal clinic in November, 1944. History and examination were satisfactory and the expected date of delivery was March 2, 1945. On December 18th, she again attended the clinic and was found to be in satisfactory condition. On December 23rd she was admitted to the maternity department complaining of extremely severe abdominal pain and vomiting. She had had vague abdominal discomfort the day before. The abdomen was tense, hard and tender, fetal parts could not be felt and the fetal heart was inaudible. The patient had felt no fetal movements since the previous day. The fundus was elevated to about 2 inches below the xiphisternum. There was no vaginal bleeding and the cervix was closed. The urine was sugar- and albumin-free.

A diagnosis of concealed accidental hemorrhage was made. Morphine was administered and the patient was closely supervised. Labor had not begun 6 hours later, the abdomen had not enlarged further, but vomiting persisted. Tense, bulging, intact membranes could be felt with the finger-tip. Labor was induced with pituitrin and stilbestrol and the membranes were ruptured with a Spencer Wells forceps. Five pints of liquor were expelled with great tension and an additional pint trickled out. It now being evident that the diagnosis of concealed accidental hemorrhage was erroneous, a diagnosis of acute hydramnios was made.

The level of the uterine fundus sank to the umbilicus and an anencephalic fetus

was delivered. The placenta weighed 5 ounces and showed no macroscopic or microscopic abnormality. The cord showed no twists to suggest obstruction. Microscopically, the epithelium of the amnion appeared less tall, more deeply stained and less vacuolated than in the controls.

The author concludes that acute hydramnios apparently occurs in patients who would, in any case, develop hydramnios slowly, but owing to the introduction of an additional factor, namely muscle which is over-sensitive to undue stretching, especially in the presence of an extra amniotic sac, and sometimes following trauma, symptoms arise acutely.

## ETIOLOGY AND TREATMENT OF HEARTBURN OF PREGNANCY

HAROLD M. WILEY

*Am. J. Obst. & Gynec.*, 51: 221-24, 1946

The persistence of even a slight degree of heartburn will tend to lower the efficiency and morale of the pregnant woman and if the condition is severe and occurs at night, preventing sleep, it can be a potential threat to the health of the patient.

Williams has summarized the changes in the stomach and its physiology during pregnancy. Changes in the position of the stomach, brought about by the encroachment of the enlarging uterus, hinder the emptying of the stomach and tend to precipitate waves of reverse peristalsis. There is also an increasing atony of the stomach musculature as pregnancy progresses. This seems to involve the cardiac sphincter as well as the lower end of the esophagus, thus permitting easy access of the gastric contents into the distal esophagus. A third major change is the diminished motility of the stomach; during pregnancy the normal emptying time may be doubled.

On the basis of these changes in the stomach during gravidity, the neuromuscular theory of heartburn has been established. According to this hypothesis, heartburn is the result of a regurgitation of gastric contents into the distal esophagus with its sensitive neural endings plus the intermittent spasm of the pyloric sphincter.

In view of the theory of disturbed neuromuscular function, it was rational to consider the use of prostigmine, which has been shown to increase peristalsis. Twenty pregnant women, complaining of heartburn, were given a supply of prostigmine bromide tablets (15 mg. each) and instructed to take one as soon as the symptom appeared. Fifteen of the women obtained complete relief within 15 minutes after taking one tablet. Two other patients reported partial relief.

The author maintains that inasmuch as the single, effective dose is so small, there is little or no likelihood of the appearance of any side reaction. Also, there is no danger of the drug causing an interruption of pregnancy.

(See Editorial Note in February issue of *Survey*, page 33.—Ed.)

PENICILLIN TREATMENT OF THE SYPHILITIC  
PREGNANT WOMANN. R. INGRAHAM, JR., J. H. STOKES, H. BEERMAN, J. W. LENTZ  
AND V. S. WATMOCK

J. A. M. A., 130: 683-88, 1946

The conclusions reached in this paper are based on a study still in progress and are subject to modification as additional information is accumulated. They do, however, represent the authors' working knowledge of the treatment of the pregnant woman with early syphilis with sodium penicillin by intramuscular injection and as such are of value as an interim report.

To date, the authors have treated 49 pregnant women with penicillin. Of these, 40 were Negro and 9 were white. Most of them were young primiparas with a recently acquired infection; the average age was 19 years. Two of the patients had primary syphilis, 24 had secondary syphilis and 19 had early latent syphilis, known to be of less than 4 years' duration. The authors also treated 3 cases of late latent syphilis and one case of congenital syphilis with interstitial keratitis.

Specific therapy during pregnancy was with penicillin only, 10 patients receiving a total dosage of 1.2 million Oxford units of sodium penicillin, 30 receiving 2.4 million Oxford units and 9 being treated individually without a definite schedule. The drug was administered intramuscularly in distilled water at 3 and 4 hour intervals. In the majority of cases the initial dosage was about one-fourth the maximum dose for the first 48 hours; subsequent dosage was from 20,000 to 50,000 Oxford units per injection. The total duration of treatment was usually from 7 to 9 days.

The only reaction of note encountered was threatened abortion. One patient with early latent syphilis, and in the 4th month of her pregnancy, aborted on the 4th day after penicillin therapy was begun, lower abdominal pain and spotting having begun on the 2nd day. Another patient, also in the 4th month, had vaginal bleeding on the 2nd day after institution of treatment and treatment was stopped on the 5th day. Abortion did not occur and she was retraced in the 7th month of her pregnancy without ill effect. It is recommended that the dosage be reduced to one-fourth during the first 24 hours and to one-half during the second 24 hours to reduce the possibility of threatened abortion from therapeutic shock.

In all instances in which the mother had evidence of early syphilis at the start of treatment, these signs and symptoms promptly disappeared. However, in only 7 instances among the 40 women who have thus far reached term had the blood serologic test become negative before the baby was born. It is concluded, from the uniformly favorable outcome, that a reversal to negative during the antepartum period is not necessary to obtain a normal infant. Only 20 of the 49 patients have developed persistently negative serologic tests. The results would seem to indicate that the pregnant woman with early syphilis, treated with peni-

cillin, may be expected to remain seropositive even though treatment is apparently effective, for as long as 6 months to one year after treatment is completed.

One syphilitic infant has occurred among 37 syphilitic pregnancies, treated with penicillin, which have reached term. In 27 of these cases the infant has been followed for periods greater than 2 months postnatally and the presumptive evidence that the infant is normal is good. This represents a degree of success equal to if not greater than that obtained with the arsenical-bismuth regimens at present widely employed.

As a result of their continued use of penicillin in the treatment of the pregnant woman with early syphilis, the authors are confident that this drug represents a distinct advantage in that it is a convenient, safe and effective mode of therapy.

(See Editorial Note following next abstract.—Ed.)

## PENICILLIN IN PREVENTION OF PRENATAL SYPHILIS

MARY S. GOODWIN AND J. E. MOORE

J. A. M. A., 130: 688-94, 1946

The authors have treated 31 mothers, all of whom had early infectious (primary or secondary) syphilis at the time of treatment, with penicillin. All have now delivered and all infants are apparently normal. The authors compare this material with the 26 out of 49 patients having lesions of early syphilis in the group of Ingraham and his associates.

Twenty-eight of the mothers in the present series received single courses of penicillin and 3 received multiple courses. The total dosage averaged from 1.2 to 2.4 million units. All 3 of the patients to whom retreatment was given during pregnancy had serologic relapses in the last trimester. In each case the infant was born alive and apparently normal. In the combined groups of Ingraham and his associates and the present authors, 14 patients were treated before the 16th week of pregnancy, 31 were treated between the 16th and 32nd week, and 12 were treated at 32 weeks or later. This distribution of cases throughout pregnancy should give a fair appraisal of the value of penicillin in any stage of pregnancy.

While Ingraham and his associates observed 2 actual and 2 threatened abortions among the 49 women treated, 3 of these were in patients with latent syphilis. This phenomenon has been interpreted as possibly due to therapeutic shock. The fact that 3 of their actual and threatened abortions were in patients with latent syphilis, coupled with the total absence in 25 of their 26 and in all of the present 30 patients with early syphilis, tends, the authors believe, to weaken this argument. If one combines a total of 101 women treated by Ingraham and his group, by Leavitt and by the authors, there were 4 actual and 7 threatened abortions. It is a well known fact in obstetrics that approximately 10 per cent of all

pregnancies in normal, nonsyphilitic, nonpenicillin treated women end in spontaneous abortion and perhaps another 5 to 10 per cent have threatened abortions.

Only 12 of the 22 patients in this series who have been followed for 6 months or longer after treatment have become seronegative. Ingraham and his associates stated, in regard to the serologic response of their 49 cases, that "the serologic response here noted is considerably slower than that recorded... for early syphilis as a whole." The authors feel that this conclusion is unjustified because of lack of separation of their material as between early and latent syphilis. The serologic response to penicillin of patients with long-standing syphilitic infection (2 years or longer) is considerably less prompt than that in early infectious syphilis.

Of the 31 women in the present series, all have delivered, with a total of 33 infants alive and apparently normal at birth. Not one of the infants has developed any clinical, serologic or roentgenographic evidence of congenital syphilis. It is noted that in the combined series of Ingraham and his associates and of the authors, 19 infants had positive blood serologic tests in cord or venous blood at birth or within the first week of life. Eighteen of these have become spontaneously seronegative.

The results in both series of patients in the prevention of prenatal syphilis are superior to any heretofore attainable with any method of treatment. It is recommended that in syphilitic pregnant women, penicillin be used routinely for the prevention of prenatal syphilis, other methods of treatment being abandoned.

(Although the word "epoch-making" has been worn rather thin from extravagant misuse, it would surely apply in its full force to the above two papers. Let obstetricians everywhere note that treatment of syphilitic pregnant women by arsenicals and bismuth is now considered obsolete in view of the superior efficacy and safety of penicillin,—this on the word of two groups of experienced syphilologists and pediatricians who have investigated the problem most thoroughly. As pointed out by Goodwin and Moore, we feel certain on the basis of our experience at the Johns Hopkins Hospital that abortion is no more common in the group of patients treated with penicillin than it is in our clinic population in general.

From a broad public health point of view, the penicillin treatment of syphilis in pregnancy represents an immeasurable advance since lapses in treatment are well-nigh impossible with a single, concentrated 7 or 10 day program of therapy. As everyone knows, lapses in treatment were very common with weekly injections of arsenic and bismuth despite legislative and punitive measures.—Ed.)

## RUBELLA IN PREGNANCY CAUSING MALFORMATIONS IN NEWBORN

M. J. FOX AND M. M. BORTIN

J. A. M. A., 130: 568-69, 1946

The congenital anomalies which have been noted in the newborn of mothers having rubella during pregnancy are cataracts, heart disease, deaf-mutism, microcephaly, microphthalmos, atresia of the biliary ducts and renal glomerulo-

sclerosis. Table 1 presents most of the authors and their publications in the recent literature.

Most of the investigators have based their conclusions on individual records, failing to cite the total number of women having rubella in pregnancy with no congenital defects in the offspring. The authors do not question that it is quite apparent that there is some relationship between these anomalies and the occurrence of rubella during pregnancy. However, they feel that the entire subject must be interpreted from a public health point of view.

A discussion is presented of the embryology of the lens of the eye, of the internal ear and of the septums of the heart. The lens of the eye first appears during the 4th week and, in association with the other structures of the eyeball, reaches its

TABLE 1  
*Recent publications on Rubella*

AUTHOR	YEAR REPORTED	NUMBER OF CASES	TYPES OF CONGENITAL MALFORMATIONS				
			Cataracts, microphthalmos	Congenital heart lesions	Deaf mutism	Microcephaly	Atresia of bile ducts
Gregg .....	1941	78	78	44			
Swan and others.....	1943	31	14	17	7	3	
Swan and others.....	1944	12	2	4	5		1
Carruthers .....	1945	18	0	1	18	3	
Reese .....	1944	3	3	3		1	
Erickson .....	1944	11	11	9			
Rones .....	1944	3	3	1			
Perera.....	1945	1	1	1			
deRoeth & others.....	1945	2	2	1			

typical appearance during the 3rd month. The appearance of the primordium of the internal ear has been observed in embryos of 3 to 4 weeks. Development continues until morphologic differentiation is practically complete in the 3rd month. Partition of the primitive chambers of the heart begins between 5 and 6 weeks. Development of the interatrial and interventricular septums is completed by the end of the 7th week. However, the interatrial septum is not entirely complete until the foramen ovale is closed at birth.

The authors present data which show that 22,226 cases of rubella were reported in Milwaukee during the 3 years of 1942, 1943 and 1944. Of these, 152 married women were investigated; 11 were pregnant at the time they had rubella. Of these 11 women who had rubella during pregnancy, the disease occurred in 5 during the first 2 months, in 4 during the 2nd to 4th month, in one in the 7th month and in one in the 9th month.

One stillbirth (hydrocephalic infant) occurred among the 11 cases; one woman had twins, both normal; one woman gave birth to a blue baby with sinus disease, otitis media and hydrocephalus which receded immediately (the child is perfectly normal at present); and the remainder of the infants were normal, having no

congenital malformations. A 12th case is included which is of particular interest. The mother, who had rubella in her 2nd month, gave birth to a normal child at term. In 1937 she had a normal pregnancy and gave birth to a child at that time with bilateral congenital cataracts.

In these 11 cases, only one evidenced a pathologic course, an incidence of 9.09 per cent. This percentage does not concur with the statement of Swan, who claims that all mothers with such exanthems during the first 2 months of pregnancy will give birth to children with congenital abnormalities. The subject deserves further careful investigation and a similar study might be made of other virus diseases.

The question of therapeutic abortion in this disease has been suggested by several sources. The authors' records do not justify consideration of termination of pregnancy because of rubella.

(More studies of this sort will be necessary before we can decide intelligently and finally upon the justification of therapeutic abortion in patients who have had rubella in early pregnancy; and meanwhile, the question must remain under judgement. Certain it is, as Fox and Bortin point out, that a goodly number of patients who have presumably had rubella in the first trimester of pregnancy, give birth to normal infants. Whether such cases are due to a mistaken diagnosis of German measles or to other factors cannot be said, but they do make us hesitate to perform therapeutic abortion routinely in these cases. On the other hand, the carrying of such patients through pregnancy is an onerous responsibility. This is particularly true if the diagnosis of rubella was definitely established, if the disease occurred around the 7th week and if an intelligent patient and her husband, dreading the thought of a blind baby, request interruption of pregnancy.)

It is regrettable that monkeys do not contract German measles more readily. Dr. George W. Corner, the well known anatomist, is attempting to investigate this problem experimentally on the rhesus macaque, but his preliminary efforts have been thwarted by an inability to inoculate monkeys with rubella.—Ed.)

## PREGNANCY IN CASES OF PITUITARY DWARFISM

GEORGE SPECK

Am. J. Obst. & Gynec., 51: 217-20, 1946

The author considers the 3 problems presented by the pregnant dwarf: (1) heredity of the physical abnormality and whether pregnancy should be advised or discouraged; (2) character of the antepartum course; and (3) management of the labor. Possible psychological complications are not discussed in this paper.

Dwarfs may be divided into 2 major types, the true dwarf and the achondroplastic dwarf. From the available literature, the true dwarfs seem invariably to give birth to normal offspring and can be told that their chance of having a dwarf child would be the same as that of normal individuals. However, achondroplastic dwarfs frequently give birth to achondroplastic babies. In the series of cases presented in this report, 53.5 per cent of achondroplastic mothers gave

birth to achondroplastic infants, indicating that there must be a hereditary factor in achondroplasia which is lacking in the pituitary dwarf. Achondroplastic dwarfs should be forewarned of the strong possibility of having an achondroplastic child.

The antepartum course of either type of dwarf does not appear to be different from that of the normal individual, although it may present certain psychological difficulties.

Since in all cases presented by the author, the pelvis were markedly contracted an elective cesarean section was performed in each instance. With this method of delivery, the management of labor will give rise to few complications.

A case report is presented of a 41-year-old white pituitary dwarf whose parents were both normal. Her mother had 11 children, the rest of whom were normal. The patient was delivered by cesarean section of a female child weighing 4 pounds, 15 ounces and measuring 16 inches in length. The baby had multiple congenital deformities and died 3 hours after delivery. An autopsy disclosed the following abnormalities: meningocele, polydactylism, congenital polycystic kidneys, congenital cystic liver, cor biloculare, atresia of urinary bladder, split tongue, prematurity and partial expansion of lungs with congestion and hemorrhage. No instances were encountered in the literature of babies born to pituitary dwarfs with congenital anomalies of this type.

## RUPTURE OF THE RECTUS ABDOMINIS MUSCLE DURING PREGNANCY

RUFUS C. THOMAS

J. Obst. & Gynaec. Brit. Emp., 52: 580-83, 1945

The author records a case of rupture of the rectus abdominis muscle during pregnancy. This is the 2nd example seen by him and the 32nd disclosed in the literature. The difficulty in diagnosis is shown by the fact that in only 9 of the 32 cases was the correct diagnosis made.

In the cases already recorded, 18 of the 31 patients had a history of respiratory trouble, acute or chronic. In 5 the onset of symptoms coincided with the strain of labor. In 2 there was the history of a fall. One occurred after labor during the course of typhoid fever, illustrating the etiological significance of muscle degeneration. Multiparity appears to be an important factor; of the 31 patients, 3 were primigravidae, 24 were multigravidae and in 4 the parity was not stated. Stretching of the rectus muscles by the enlarging uterus appears also to be a factor since all of the cases reported have been in the 2nd half of pregnancy, the majority being within 8 weeks of term.

In 5 instances Cullen's sign was present. The significance of this sign, if the possibility of hemorrhage into the rectus sheath is borne in mind, is obvious.

The condition carries a maternal mortality of 13 per cent and a fetal mortality

probably in the region of 50 per cent. It must, therefore, rank with the other hemorrhages of late pregnancy in danger to mother and child.

The number of cases reported would seem to imply that the condition is rare. It is probably true that "a great number of h matomas of the rectus muscles in pregnancy are small, unnoticed and undiagnosed, and consequently unreported."

In regard to treatment, the literature shows that 21 patients were operated upon, with evacuation of the clot, and that in 3 instances the bleeding vessel was found and ligatured. In 4 of these cases, cesarean section also was performed. The author believes that conservative treatment is justified only so long as the general condition remains good and there is no increase in the size of the tumor or of the abdominal pain. If the symptoms point to increase in hemorrhage, he feels that operative intervention is urgent. Such treatment is far more likely to avert a fatal issue even granted the ease with which blood transfusions can be given nowadays.

### MELANCHOLIC DELIRIUM WITH HALLUCINATIONS IN A WOMAN EIGHT AND ONE-HALF MONTHS PREGNANT; RAPID CURE BY THREE ELECTRIC SHOCKS; TRANSIENT MODIFICATION OF FETAL HEART BEATS

LEROUX, CORMAN AND LONGUET

Gynec. et obst., 44: 186-88, 1945

The patient, a 34-year-old woman, entered the hospital at about 8½ months of her 2nd pregnancy in a deranged mental state. The symptoms had begun 8 days previously and had progressed to a depressive state with muteness, almost complete physical and psychic inertia and auditory hallucinations. The pregnancy was normal in all respects. The mental state was atypical; the patient showed a melancholic delirium with very intense auditory hallucinations and expressed ideas of killing everyone near her. The prognosis was grave because of a suggested hereditary factor; the patient's sister had been hospitalized for 10 years for precocious insanity.

The most indicated form of treatment appeared to be electric shock. Three treatments were administered with a complete cure. At each application of the electric shocks, the fetal heart beats were modified and muffled and, about one minute afterward, they became irregular in rhythm. These changes were transient, disappearing in about a minute. The functions of the general organs of the patient were not disturbed. Particularly, the uterus was not influenced in the least by the electric shocks. Delivery took place normally and spontaneously at term with a resulting well developed infant.

The electric shock needs no further proof of its therapeutic value in mental ailments. However, it is interesting to know with what impunity it can be used in the treatment of the pregnant woman who has a mental derangement.

## PREGNANCY COMPLICATING MULTIPLE SCLEROSIS

J. IRVING KUSHNER

*Am. J. Obst. & Gynec.*, 51: 278-79, 1946

It is a well established clinical fact that multiple sclerosis is frequently made worse by pregnancy. The author presents a case which is of interest because of the improvement of neurological signs after delivery.

The patient became pregnant  $2\frac{1}{2}$  years after the onset of the multiple sclerosis. The neurological findings at the 3rd month of gestation were as follows: marked nystagmus, intention tremor, absent abdominal reflexes, and spasticity and weakness of both extremities. Her prenatal course was normal. She was delivered of a normal child and the postpartum course was uneventful.

Three months later a postpartum examination noted the following neurological changes for the better: nystagmus only slight in the lateral position, increase in strength on the left leg, intention tremor much less pronounced. Examination 2 years after delivery showed no progression in the neurological findings.

(The evidence is growing that in the majority of cases pregnancy has no effect on the course of multiple sclerosis and that it is rarely an indication for therapeutic abortion. It is true that many cases have been reported in which the condition seemed to have been aggravated by pregnancy; but it must be borne in mind that multiple sclerosis in the non-pregnant state is characterized by unexplained exacerbations and alternating quiescent periods, and that any change for the worse observed during gestation might well have developed just the same in the absence of pregnancy. The last four cases of multiple sclerosis complicated by pregnancy which I have followed did very satisfactorily. Most of these patients, as is understandable, have less pain in labor than usual and in some the labors are almost painless.—Ed.

## MYASTHENIA GRAVIS AND PREGNANCY

A. WILSON AND S. J. BARR

*J. Obst. & Gynaec. Brit. Emp.*, 52: 584-88, 1945

The relative rarity of myasthenia gravis associated with pregnancy is demonstrated by the fact that between 1900 and 1940, of 63,268 admissions to the Boston Lying-In Hospital, only one case of myasthenia gravis was registered. The literature shows various observations on patients having this disease associated with pregnancy. Some report an unfavorable effect of pregnancy or even labor and the puerperium on myasthenia gravis while others have observed no change or some improvement. Before prostigmin became available for treating the disease, it was the practice to recommend termination of the pregnancy. The consensus of modern opinion is entirely against this procedure. It was probably not realized sufficiently in former times that the course of myasthenia gravis is

characterized by periods of relapse and remission. Since the introduction of prostigmin in the treatment of myasthenia gravis, it has become possible to assess more accurately the question of relapse and remission during pregnancy according to the amount of prostigmin required for satisfactory maintenance.

The author presents the case of a 28-year-old woman, first seen in July, 1942, with the complaint of tiredness, difficulty in chewing and swallowing, diplopia and drooping of the right eyelid. The symptoms had begun a year previously. Prostigmin was instituted and she was satisfactorily maintained by 15 mg. 3 times a day and ephedrine  $\frac{1}{2}$  gr. twice daily. In November, 1943, she became pregnant and at the beginning of the 2nd trimester she found it necessary to take 60 mg. of prostigmin daily. She continued on this dose until the end of pregnancy. Labor began spontaneously and was normal with the delivery of a normal child. A definite remission of signs and symptoms was observed on the 9th day of the puerperium which continued for 9 months.

It is concluded that there is no indication that pregnancy, labor or nursing adversely affects the course of myasthenia gravis in a patient treated with prostigmin and ephedrine.

## ANEURYSM OF THE SPLENIC ARTERY WITH RUPTURE, A RARE COMPLICATION OF PREGNANCY

W. C. DANFORTH

Am. J. Obst. & Gynec., 50: 753-56, 1945

The author reports the following case which illustrates a complication extremely rare during pregnancy.

A 28-year-old woman entered the hospital at the end of the 7th month complaining of severe upper abdominal pain. Abdominal and pelvic examinations were negative, but all the usual signs of severe blood loss were present. Because her condition became worse, the uterus was emptied by vaginal hysterotomy. A dead fetus was removed but no sign of premature detachment of the placenta was found. About midnight of this day, sudden collapse was followed by death. The autopsy disclosed a massive hemorrhage into the peritoneal cavity. An enormous retroperitoneal hematoma was found extending up to the level of the kidney. The aneurysmal sac was 1.5 cm. in diameter and contained clotted blood adherent to its lining. The wall of the aneurysm showed areas of necrosis.

Published reports indicate that aneurysm of the splenic artery is most frequent in the 3rd decade. A study of the reported cases would indicate that calcification of the arterial wall, with attendant weakening, is of etiological importance. Ponfick suggests that endocarditis is equally important in this respect.

While the condition is not a common one, it occurs with sufficient frequency to make a familiarity with its symptoms desirable. There are 13 cases in the entire available literature since 1939. The 3 suggestive signs of splenic aneurysm are:

(1) left upper quadrant pain; (2) a systolic bruit over a palpable tumor mass; and (3) a pulsating filling defect in the greater curvature of the stomach as shown by x-ray.

If surgical therapy is to be attempted, it should be either the removal of the aneurysm, with the excision of the spleen as well, if necessary, or the ligation of the splenic artery. Tamponade is unsatisfactory and is accompanied by a high mortality.

## PATHOLOGY OF LABOR AND PUERPERIUM

### THE ROLE OF PORRO CESAREAN SECTION IN MODERN OBSTETRICS

KARL M. WILSON

Am. J. Obst. & Gynec., 50: 761-64, 1945

The author presents a series of 31 women in whom cesarean section followed by supravaginal amputation of the uterus (Porro cesarean section) was performed. The maternal results were uniformly good, there being no maternal deaths. There were 10 (32.2 per cent) stillbirths or neonatal deaths. None of these can be attributed to the operation as 7 of the infants were known to be dead at the time of operation. Two mature infants died of atelectasis and one infant of prematurity.

This operative procedure still has an important place in obstetric operative procedures, though the necessity for it has decreased following the introduction of other techniques such as low cervical cesarean section and the various forms of extra-peritoneal operations. Also, with improved prenatal care and increasing hospitalization of obstetric patients, fewer neglected cases are seen.

The particular indications for removal of the uterus after cesarean section are found to be: (a) Myomatous uteri containing myomas of such a size and in such a position as to necessitate cesarean section in the first place, and when myomectomy is precluded. (b) Uncontrollable hemorrhage when removal of the uterus is necessary as an emergency lifesaving measure, often in association with abruptio placentae but occasionally encountered apart from this. (c) The presence of frank intrapartum infection when cesarean section is done. It is in this group that a decrease in the necessity for removal of the uterus has occurred and further reduction should be possible. (d) As a means of effecting sterilization when it is indicated and where, for some reason, it may seem preferable to remove the uterus rather than to resect the tubes.

No examples of ruptured uterus requiring hysterectomy are included in this series, as this would seem to be an entirely separate problem.

(It is my own feeling that the judicious use of penicillin in every case in which intrapartum infection is either an actuality or a threat will go far to eliminate the necessity both of cesarean-hysterectomy done for infection and extra-peritoneal cesarean section. Certainly in the past two years, with the aid of penicillin, we have done a substantial number of low cervical operations on infected and potentially infected cases, in which we would previously have performed either the Porro or Waters type of operation; and the post-operative courses of these cases have been amazingly afebrile, without a suggestion of peritoneal irritation.—Ed.)

## EXTENSIVE VARIX OF THE VULVA AND VAGINA IN FULL-TERM PREGNANCY; DELIVERY BY CESAREAN SECTION

SAMUEL S. ADLER

Am. J. Obst. & Gynec., 51: 272-74, 1946

Varix of the vagina alone or in combination with those of the vulva is a rare lesion complicating pregnancy. Such genital varicosities may give rise to considerable hemorrhage should they rupture during the course of labor. The purpose of this paper is to report a case, to indicate the dangers of vaginal delivery in the presence of extensive genital varices and to emphasize that the treatment of choice in such cases is elective cesarean section.

A 20-year-old white patient was examined in the 4th month of her pregnancy and found to be essentially normal. Toward the end of the 6th month she complained of swelling of the legs, pain in the left leg and aching in the vagina. Examination revealed moderately severe varicose veins, more pronounced in the left leg. There were extensive bilateral varicosities of the labia majora and minora and a large, soft, purplish varicose vein bulging through the vestibule which extended along the right margin of the posterior vaginal floor. As pregnancy progressed the genital varices became more pronounced and, fearing rupture if she were permitted to go into labor, an elective low classical abdominal section was performed. A complicating postpartum phlebitis of the left saphenous vein was treated by x-ray therapy. Six weeks after delivery the thigh and legs showed only an occasional fine varicose vein and no varices of the vulva or vagina were noted.

(It is possible that the genital varicosities in Adler's case were so extreme in degree as to justify abdominal delivery but, in general, varices of the vulva and vagina rarely call for cesarean section. The condition is not uncommon in women of great parity and we see some rather severe examples of it, especially among our ward patients. Yet we have never performed a cesarean section on this indication nor have we had serious difficulty from bleeding at the time of delivery.—Ed.)

## RUPTURE OF THE UTERUS AFTER ISTHMIC LIGAMENTOPLEXIS WITH SILK, WITH A BAFFLING SYMPTOMATOLOGY

J. BRET

Gynéc. et obst., 44: 325-27, 1945

The 35-year-old patient whose case is reported in this paper had had 2 previous pregnancies terminated at term, in 1931 and 1936, respectively. In 1943 she had been subjected to an appendectomy, removal of a cyst of the left ovary and

an isthmic hysteropexia in which, according to the surgeon's statement, 2 threads of silk were passed very low on the isthmus. On January 20th, 1945, in the 8th month of her 3rd pregnancy, she was taken to the hospital for what appeared to be an insertion of the placenta on the inferior uterine segment. The symptoms had begun 2 weeks previously in the form of slight hemorrhage of red blood which responded to rest and opiates. On the day of admittance to the hospital she had had an abundant hemorrhage (about 500 grams). On examination 5 hours later, the following were noted: a high cephalic presentation, a dilatation at 2 franks and torn membranes. Two and a half hours later the dilatation had increased to 5 franks and the blood loss, which had abated, again increased to over 500 grams. A transfusion of 300 grams was given, but blood loss continued (180 grams in a half hour). Some shock phenomena appeared an hour later. At examination in another 2 hours, a mass which looked like the placenta was noticed in the dilated cervix. A diagnosis of placenta previa was made and a cesarean section was performed. On opening the abdominal cavity a white, very hard, cylindrical strap, 1.5 cm. in diameter, was found between the parietal peritoneum and the lower part of the body of the uterus. In the abdominal wall a very tight, but free, knot of silk thread was found. To the right and above the uterine implantation of the strap, the preuterine peritoneum presented a reddened circular area of 3 to 4 cm. in diameter which at first gave the impression of a placental rupture. This was confirmed at histological examination. It was concluded that during the ligamentopexy, the upper thread had been passed at the level of the body of the uterus and was responsible for the rupture. A hysterectomy was followed by an uneventful postoperative course. The infant survived. 2 figures.

## THE USE OF QUININE IN OBSTETRICS

PIERRE MOULLE

Gynéc. et obst., 44: 192-95, 1945

Quinine is an alkaloid which acts in suppressing, toward the end of pregnancy, the muscular inhibition of the uterus. It does not act directly as a stimulant but, by this suppressive process, permits an augmentation of the function of the uterine muscle and allows longer, stronger and more frequent contractions. Two conditions appear necessary to this action: (1) the use of weak doses of quinine; and (2) the gravid state of the uterus: the action manifests itself only at the end of pregnancy or in the course of labor already started.

The recommended oral dosage of the sulfate of quinine does not exceed 1 gr. 50 a day. Quinine can be administered to all patients without contraindications.

The appearance of signs of intolerance will indicate a decreased dosage or discontinued administration.

The author presents the results from the administration of quinine to various groups of patients. In 11 out of 17 cases of miscarriage, quinine appeared to have an effect. There were 3 failures out of 15 cases in which quinine was administered at term to instigate labor. In 125 instances where quinine was used during prolonged labors, the effect was clearly demonstrated in 102 cases and weak or missing in 25. The most interesting, and the most difficult to interpret, were the results in the routine administration of quinine to 42 women during the last 3 weeks of pregnancy. The results were favorable with the patients having rapid and quiet deliveries.

It is concluded that the role of quinine is particularly satisfactory at different times during delivery. It can be used as an adjuvant with the posterior pituitary hormone. It can be substituted in numerous cases of feeble labor. It can, above all, be administered prophylactically to permit a rapid and uneventful delivery. It is this last point which the author wishes to emphasize.

## DYSTOCIA DUE TO PELVIC KIDNEY

IRVING SIEGEL

*Am. J. Obst. & Gynec.*, 51: 280-81, 1946

Pelvic kidney, as one of the rare causes of dystocia, is illustrated in the following case report.

The first examination of the patient took place 6 weeks before term and at that time the external measurements were compatible with a roomy pelvis; the outlet was normal. Presentation was by breech and remained so for the remainder of pregnancy.

During labor the pains were never very hard but the cervix dilated nicely and, after 10 hours, rectal examination revealed almost complete dilatation. In the hollow of the sacrum could be felt a firm smooth mass which was assumed to be the baby's buttocks. After delay in descent of the breech, a vaginal examination was done and the mass was felt distinctly not as a part of the fetus. It was decided that breech delivery from below was impossible due to the encroachment of the mass on the pelvic cavity. A cesarean section was performed and a normal child was delivered. Palpation of the left renal fossa revealed no kidney present and the mass was assumed to be an ectopic kidney. The postoperative course was entirely uneventful.

A retrograde pyelogram revealed normal right kidney and ureter. The left kidney was in the pelvic cavity with its ureter about half the normal length. Both kidneys had normal function and no evidence of infection. 1 figure.

## PUERPERAL STERILIZATION

RICHARD VAN DYCK KNIGHT

Am. J. Obst. &amp; Gynec., 51: 104-08, 1946

The author concludes that postpartum sterilization is a rational and safe procedure when indicated. Cases for this procedure should be selected with care. The 4th or 5th postpartum day is the safest time for performing this operation.

A total of 51 puerperal sterilizations performed at the Sloane Hospital for Women from 1938 to 1944 are reviewed. The average age of the patients was 32.8 years. The 3 most common indications for the operation were multiparity (having 3 or more living children), rheumatic heart disease and recurrent toxemia. No routine type of anesthesia was used but intravenous pentothal, gas, oxygen and ether were chiefly employed. The Pomeroy sterilization was used exclusively with one known failure which is reported in another communication. A short vertical incision and absorbable suture material were used throughout. Twenty-three, or 46 per cent of these patients were entirely afebrile throughout the puerperium. The majority of the operations were performed on the 3rd, 4th and 5th days.

THE ROUTINE USE OF STILBESTROL FOR ENGORGEMENT  
AND LACTATION IN NONNURSING MOTHERS

SAMUEL LUBIN

Am. J. Obst. &amp; Gynec., 51: 225-29, 1946

The present study was made in an effort to determine the value of the routine use of stilbestrol in the prevention of engorgement, with its attendant pain, and lactation in nonnursing mothers.

One hundred nonnursing mothers were divided into 2 groups of 50 each, one of which received stilbestrol (diethylstilbestrol), and the other, a control group, which received no stilbestrol. In the former group stilbestrol was started orally within 24 hours of delivery; the dosage was 10 mg., 3 times a day, for 2 days, followed by 5 mg., 3 times a day for the remainder of the patient's stay in the hospital.

The observations recorded included the noting of pain, engorgement, milk, fever and erythema of the breast.

In the group receiving stilbestrol, engorgement was present in 50 per cent. The degree of engorgement was: filling in 20 per cent; full in 22 per cent; and hard in 8 per cent. Pain was present in 12 per cent, but relief of pain was not required by any in this group. Colostrum leakage was uniformly absent in this group but colostrum could be expressed from the breasts of 78 per cent of the

patients. Milk could be expressed, where there was no milk leakage, in 56 per cent and leakage was present in 34 per cent. Therefore, as manifested by leakage or expression of milk, lactation was present in 90 per cent of the group. Fever, present in one patient, could not be attributed to the breasts and erythema was not noted in any patient. It is of interest that 50 per cent of this group developed full, painful breasts within 2 weeks after leaving the hospital.

In the control group receiving no stilbestrol, engorgement was present in 82 per cent. The degree of engorgement was: filling in 4 per cent; full in 34 per cent; and hard in 44 per cent. Pain of varying degree was present in 42 per cent and was sufficiently severe to require relief in 25 per cent of these. Colostrum leakage was absent in all patients but colostrum could be expressed from the breasts in 84 per cent. Milk could be expressed, where there was no milk leakage, in 24 per cent, and milk leakage was present in 76 per cent. Therefore, as manifested by leakage or expression of milk, 100 per cent lactated. Fever, present in 10 per cent, could not be attributed to the breasts and erythema was not noted in any of these patients.

The author concludes that the oral administration of stilbestrol in nonnursing mothers appears to prevent engorgement of the breasts with its attendant pain and that lactation is inhibited to a slight degree. However, in many instances, engorgement is merely postponed. The advisability of routinely administering stilbestrol to nonnursing mothers for the prevention of painful, engorged and lactating breasts is questionable.

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not been tried before) adrenalin in sufficient quantity will cause a further quickening of the pulse.

The earliest date at which stimulation of the peripheral end of the right vagus was observed to slow the heart was the 77th day. On the 85th day peripheral stimulation of the left vagus also failed, but succeeded on the 101st day. Central stimulation of the left vagus, with the right vagus intact, produced slowing on the 77th day.

Slowing of the heart synchronous with rise of arterial pressure has been observed on the 111th day. Slowing of the heart which bears evidence of being reflex has been obtained by raising the blood pressure (clamping the cord) on the 121st day and by injection of adrenalin on the 118th day.

Approaching term both the carotid sinus and cardiac depressor mechanisms are functional.

Lowering of the blood pressure as the result of stimulation of the central end of the vagus and with both vagi severed can be demonstrated late in gestation. 7 figures.

(In Clement A. Smith's recent book, "The Physiology of the Newborn Infant"—an excellent monograph, by the way, published by Charles C. Thomas—the name of Sir Joseph Barcroft appears more than that of any other author. This is as it should be because the contributions of Sir Joseph and his associates to this subject, particularly to the dynamics of the fetal circulation and respiration in utero and at birth, are classics of experimental research. The present paper in which a new technique is described, brings the findings in the fetal sheep more in line with those in the human fetus than were true of his earlier observations with the mercurial manometer.

The blood pressure of the human fetus, like that of the sheep, is very low, but rises progressively from the middle of pregnancy to term. Thus, Woodbury, Robinson and Hamilton (*Am. J. Phys.*, 122: 472, 1938), have found that the pressure within the umbilical artery at the time of premature birth and at term, is as follows: 5 mos., 39/21; 6  $\frac{1}{2}$  mos., 55/25; 7 mos., 70/35; 8 mos., 85/45; 9 mos., 80/46. The last figure is based on 24 normal term infants immediately after birth.

All investigators agree that the systolic pressure increases by some 10 mm. Hg. during the first 24 hours of life and by another 10 mm. between the 1st and 10th days.—Ed.)

## THE OBSTETRICIAN'S RESPONSIBILITY FOR THE HAZARDS OF THE FIRST FEW DAYS OF LIFE WITH SPECIAL REFERENCE TO ANOXIA AND PREMATURITY

ALFRED C. BECK

*Am. J. Obst. & Gynec.*, 51: 173-83, 1946

The author has reviewed the last 5 years' records of the deliveries of all infants who reached the period of viability, with the view to ascertaining for this presentation how infant mortality might be lowered at the Long Island College Hospital.

## THE NEWBORN

### BLOOD PRESSURE AND PULSE RATE IN THE FOETAL SHEEP

J. BARCROFT AND D. H. BARRON

J. Exper. Biol., 22: 63-74, 1945

The authors describe a method for the measurement of the pressure in the stream going through a vessel. This is called the needle method. A hypodermic needle is fitted with a piece of translucent bicycle valve tubing of about a metre in length, with a small glass funnel at the other end. The system is filled with "Heparin Ringer" solution from the tip of the hypodermic needle to a distance up the tube necessary to form a column somewhat higher than represents the blood pressure measured in Ringer's solution. A forceps is placed on the rubber tubing to prevent any passage of the fluid along it. When the blood pressure is measured, the funnel is suspended to such a height that when the needle point is thrust into the vessel and the clip removed, the solution will run into the circulating blood and not the blood into the tubing. The meniscus in the tube shows oscillations produced by the heart beat or otherwise. With an ordinary wooden scale, the measurement is made of the difference of level between the meniscus and the surface of the saline bath in which the fetus lies, a correction being applied for the depth to which the fetal heart is below the saline.

In the fetal sheep, the needle method applied to the umbilical artery gives substantially the same results as the mercurial manometer applied to the carotid, until about half-way through the gestation period. As gestation proceeds, the needle method applied at the first moment at which it can be applied to the umbilical artery (or a branch) gives readings substantially lower, and increasingly lower as gestation proceeds, than does the mercurial manometer read at the first moment at which it can be read. The discrepancy is due to the sum of a number of causes which are discussed, but of these the most important is an actual rise of pressure between the time of delivery and the completion of the dissections contingent on the use of the mercurial manometer.

The cause of this is not at present demonstrated, but either or both of 2 factors may be concerned: (1) a dulling of the central nervous system which weakens the depressor reflex; (2) the establishment of a greater degree of vasomotor tone consequent on the bombardment of the central nervous system with sensory stimuli.

The pulse rates *in utero* and just after delivery of the fetus into a saline bath at 39-40 degrees C. (the umbilical circulation being unimpaired) are not significantly different. The pulse rate quickens up to the 70th-80th day, after which it becomes slower as gestation proceeds.

If both vagi be severed, the pulse rate tends to quicken throughout gestation. The pulse, therefore, becomes increasingly under vagus inhibition from the 80th-90th day onwards. Even after the vagi have been cut after the 120th day (it has

not been tried before) adrenalin in sufficient quantity will cause a further quickening of the pulse.

The earliest date at which stimulation of the peripheral end of the right vagus was observed to slow the heart was the 77th day. On the 85th day peripheral stimulation of the left vagus also failed, but succeeded on the 101st day. Central stimulation of the left vagus, with the right vagus intact, produced slowing on the 77th day.

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*Am. J. Obst. & Gynec.*, 51: 173-83, 1946

The author has reviewed the last 5 years' records of the deliveries of all infants who reached the period of viability, with the view to ascertaining for this presentation how infant mortality might be lowered at the Long Island College Hospital.

The fact that nearly 60 per cent of premature and full-term neonatal deaths occurred within 24 hours of birth indicates that the responsibility for these cases rest almost entirely upon the obstetrician. Anoxia and prematurity were found to be the commonest causes of neonatal deaths.

The author discusses the mechanism by which oxygen and carbon dioxide are exchanged between the fetal and maternal circulations. Experimentation with the rabbit shows that the transmission of oxygen by the maternal blood through the placental site does not increase in proportion to the increasing demands of the developing fetus. This condition is compensated for, to some extent, by an increase in the ability of the fetus to absorb oxygen since the oxygen capacity of fetal blood is 20.8 volume per cent as compared with an oxygen capacity of 15.4 volume per cent for maternal blood. A large maternal hemorrhage might so reduce the oxygen carriers in the mother's blood as to cause asphyxiation of the fetus in utero. In the interest of the child, accordingly, phlebotomy is contraindicated in eclampsia, and such cases of placenta previa should receive a blood transfusion before pregnancy is interrupted and the fetus is subjected to further diminution of its oxygen supply. Oxygen administration and transfusion immediately after birth may benefit the child. It is suggested that some fetuses might be saved by more frequent use of oxygen in treating pneumonia and decompensation in cardiac diseases. Sedative drugs and anesthetics may also cause intra-uterine anoxia and asphyxia or depress the fetal respiratory center so that respiration after birth is impaired. Alterations in the pressure head at the placental site may prevent the fetus from obtaining its full requirements. This observation indicates that attempt should be made to diminish the violence of uterine contractions in cases of precipitate labor and that posterior pituitary extract should be used during labor with great caution or not at all.

The author presents the most important ways in which the obstetrician may aid in the reduction of premature mortality. They are as follows:

1. Adequate supervision of the hygiene of pregnancy.
2. Proper advice regarding diet, coitus, rest and exercise.
3. Immediate notification of obstetrician upon appearance of untoward symptoms.
4. Early discovery and treatment of syphilis.
5. Prevention of congestive failure in cardiac cases.
6. Determination of size of child by means of x-ray and consultation before interrupting pregnancy.
7. Elimination of morphine, scopolamine, barbiturates and general anesthesia in all premature labors.
8. Administration of vitamin K to mother and infant.
9. Preservation of membranes as long as possible and episiotomy to protect premature infant from pressure effects of labor.
10. Spontaneous delivery of second twin and avoidance of version and extraction wherever possible.
11. Postponement of tying cord until it stops pulsating.
12. Reception of newly born premature infant in tub of warm water to prevent chilling while waiting for cord to stop pulsating.

The author discusses the cause and prevention of pressure effects on the head of the premature infant.

The results of the various methods of delivery on premature infants are compared. Breech delivery is found to be most dangerous because in young prematures the circumference of the shoulders and body is less than the circumference of the fetal head. Whenever the child is under 2000 grams, breech delivery is an extremely dangerous method. Spontaneous vertex delivery accompanied by episiotomy under local anesthesia is the safest method of delivery for premature infants. Cesarean section is not a dangerous but a valuable method of delivery. The high premature infant mortality which is recorded for this operation usually is due to the maternal or fetal complication which serves as the indication for the operation rather than to the method of delivery.

## INITIAL FETAL ATELECTASIS

HENRY J. ZETTELMAN

*Am. J. Obst. & Gynec.*, 51: 241-45, 1946

Whether the human fetal lung is atelectatic until birth is a question which has been debated for many years. In 1888, Ahlfeld described rhythmic fetal movements observed in patients during the latter weeks of pregnancy. He suggested that this activity was due to respiratory efforts and thought that aspiration of the amniotic fluid must occur. It has been stated: "There is evidence that intrauterine respiration is of a functional significance in the development of a normal lung, aiding in dilatation in alveoli and elastic walls of the future air passages." The injection of radiopaque material into the amniotic sac of experimental animals has resulted in the appearance of the radiopaque material in the lungs of the animal only when anoxemia was present. Experimental work on humans has proved that aspiration of amniotic sac contents can occur. The evidence available at present seems to indicate that fetuses are apneic during the greater part of gestation, and that fetuses whose oxygen requirements are adequately met are apneic until birth.

This paper briefly presents congenital anomalies in 2 stillborn fetuses which may clarify the structural picture of the lung just before birth. The pathologic reports revealed that both of these fetuses were premature anencephalic infants. The lungs of both showed complete atelectasis; they were compact, glandlike organs whose respiratory passages were not filled.

The supposition has been made that fluid contained in the fetal lung of experimental animals is coextensive with that in the amniotic cavity. This cannot be proved as a normal condition because it is possible that, during the death of the fetus in utero, asphyxial conditions had induced intrauterine respiratory movements and led to aspiration. The significance of the 2 cases cited in this paper is that a marked anencephalus was present in each case, suggesting a

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definite disturbance if not actual lack of central nervous system control of the body. Hence, it is highly probable that the fetuses, in the final agonal movements preceding death, were not able to make the dyspneic gasps observed in anoxic experimental animals. Therefore, the lungs were in the condition of a normal birth at term, namely, in the state of atelectasis. It is suggested, as a result of this study, that the initial atelectasis of the fetal lung persists in man until birth.

(Before very long, probably before this issue of the Survey reaches you, a most important study from one of the large Chicago clinics will be published on this subject. It will show beyond peradventure that radiopaque material, when injected into the normal human pregnant uterus, becomes widely dispersed throughout the lungs even very early in pregnancy. This evidence seems irrefutable and, in my opinion, should well-nigh settle this old controversy on fetal respiratory movements in favor of their existence as a normal, physiologic phenomenon.—Ed.)

## THE RH FACTOR IN OBSTETRICS

H. F. TRAUT, B. C. McIVOR, ET. AL.

Am. J. Obst. & Gynec., 50: 722-34, 1945

The significance of the Rh factor in obstetrics makes it important that the obstetrician understand, in so far as is possible, the various elements of the problem which this characteristic of the red blood cell imposes upon us.

Much progress has been made since the announcement of the Rhesus blood factor by Landsteiner and Wiener in 1940. Other investigators, including Dienst, Murray, McQuarrie, Ottenberg, Gruhitz, Allen and Darrow approached the matter from various points of view before that time. In 1940, Landsteiner and Wiener demonstrated an agglutinin in the blood of the Rhesus monkey. After injecting monkey blood into rabbits, the serum of the latter contained agglutinins capable of reacting with a high percentage of human red blood cells. These agglutinogens were designated as "the Rh factor" because it was found to be a constant characteristic of the red blood cells of the Rhesus monkey. Those human cells which were not agglutinated by the antirhesus serum were designated as Rh negative, whereas those which were agglutinated by it were called Rh positive. Wiener and Peters, in 1940, made the first practical application of the Rh immunizing principle and in the same year Levine demonstrated that a number of women who had had repeated abortions possessed blood sera in which isoagglutinins similar to the Rh factor were present. This ultimately led to the hypothesis that erythroblastosis fetalis is the result of the formation of Rh agglutinins on the part of the Rh-negative mother either as the result of transfusions of Rh-positive blood or the harboring of a Rh-positive fetus.

Altogether more than 12,000 individuals have been tested with the results showing about 85 per cent to be Rh-positive and about 15 per cent to be Rh-negative. There were found to be racial differences, the white race having the lowest percentage of Rh-positive individuals. It has been shown that the Rh-positive characteristic is inherited as a dominant in the Mendelian manner. In a study of 60 Rh-negative women, it was shown that of the Rh-negative matings, 100 per cent were Rh-negative. In the matings of Rh-positive husbands and Rh-negative wives, 29 per cent of the offspring were Rh-negative, indicating that probably some of the husbands were heterozygous. It has also been shown that there are many possible types of Rh positivity, the meaning of which remains to be studied.

The Rh characteristic develops early in life; it has been demonstrated as early as the 12th week of life. Rh agglutinins are not normally found in the human body and must either be transmitted passively by transfusion or be generated actively as a result of transfusion or pregnancy. The response varies, depending on the antigenic potency of the red blood cells introduced as well as the ability of the recipient to produce immune bodies. In general, the relation of mother and fetus in pregnancy provides a more favorable background for the development of Rh antibodies than does transfusion alone. Whatever the mechanism may be for providing an intermixture of maternal and fetal blood elements, it has been shown that the Rh-negative mother carrying an Rh-positive infant will frequently, more often after the first pregnancy, develop Rh antibodies which she may transmit to her progeny by way of the placenta.

It is a pathologic speculation that there are 2 general types of reactions, red blood corpuscle destruction with its sequelae on the one hand, and hydrops on the other. These may be interrelated and interdependent. It is felt that icterus gravis and fetal hydrops are alternate expressions of the effect of the Rh antibodies upon the fetal tissues. In the authors' experience, it seems that a number of subclinical evidences of hemolytic disease should receive careful scrutiny in this connection. They are: enlarged spleen, enlarged liver, nucleated red blood cells in excess of 5 per 100 white cells, jaundice, bleeding tendencies, anemias, hydrocephalus and spontaneous miscarriage or abortion.

In a group of 110 Rh-negative mothers, 66 Rh-positive offspring were born. Of this group, erythroblastosis was diagnosed 7 times. In addition to the frankly erythroblastotic infants there were 9 with definite suggestive abnormalities, making a total incidence of abnormality of 24 per cent. There were also 3 incidences of subclinical abnormality.

The study of anti-Rh titers is suggestive only in the sense that the intensity and timing of the maternal reaction may bear some relation to the effect of the antibodies upon her offspring.

It is known that the relationship of Rh-positive mothers and Rh-negative fathers may be associated with fetal inheritance, bringing into play agglutinogens to which the mothers react in a manner deleterious to the offspring.

The first requirement in the treatment of newborn infants having hemolytic

disease is that couples be forewarned. It has been suggested that pregnancies be terminated before the end of the 10th lunar month but the helpfulness of this is doubtful since more infants die neonatally than are stillborn and one would have the further handicap of prematurity. The avoidance of any means of analgesia or anesthesia which is associated with a decreased oxygen-carrying capacity in the maternal blood is important. At present, the most important feature in the treatment of hemolytic disease is prompt transfusion of the infant with Rh-negative blood from a donor other than the mother. Red blood cell counts done on cord blood as soon as the infant is born should be routine on all infants of Rh-negative mothers. Oxygen therapy has proved to be of some assistance, particularly in the icteric and anemic groups of infants, and especially if the red blood count be markedly reduced.

## THE ASSOCIATION OF ERYTHROBLASTOSIS FOETALIS AND ACCIDENTAL ANTEPARTUM HAEMORRHAGE

A. E. BURCH

J. Obst. & Gynaec. Brit. Emp., 52: 463-67, 1945

The mode of passage of the Rh antigen from the maternal to the fetal circulation thought to be confined to the red cells, has puzzled everyone. In 2 out of 3 cases of erythroblastosis occurring in 6 months at Queen Charlotte's Hospital, there was premature separation of the normally implanted placenta with antepartum hemorrhage. It seemed possible that the hemorrhage from the placental site with rupture of the maternal sinuses and consequent damage to the placenta might be the factor allowing transmission of antigen and agglutinins. Since both premature separation of the placenta and erythroblastosis are comparatively rare, these facts suggest that the association might be one of some significance.

An investigation was made of all cases of antepartum hemorrhage occurring at St. Alfege's Hospital between February and June, 1945. Five out of 10 (50 per cent) of the mothers who had an accidental antepartum hemorrhage were Rh negative with Rh positive husbands and 3 of these had anti-Rh agglutinins. Of the 3 who were delivered soon after the antepartum hemorrhage, one had a child with a moderate degree of jaundice, another a child with very gross hydrops and the 3rd a child stillborn, possibly as a result of the course of labor. In the 2 mothers who were not delivered until some weeks after the first hemorrhage, the fetus was stillborn, macerated and of a size corresponding roughly with death at the time of the onset of bleeding.

It is too early to dogmatize, but the author considers it justifiable to conclude that the woman in whom iso-immunization can occur, is abnormally prone to

accidental antepartum hemorrhage, and the ensuing placental damage may be a factor in transmission of antigen and agglutinin.

## CONVULSIONS PRODUCED BY FETAL ANOXIA; EXPERIMENTAL STUDY

F. A. FENDER, W. B. NEFF AND GRACE BINGER

Anesthesiology, 7: 10-13, 1946

The authors' interest in the possible relation between anoxia and the convulsive state began with the observation that many patients suffering from convulsions had complicated birth histories. Nervous tissue is more sensitive to lack of oxygen than any other type of tissue, corresponding to the following gradient: the gray matter of the cerebrum and cerebellum requires the most oxygen, the white matter less and the spinal cord least of all. The implication is that levels believed to be responsible for convulsions or "epilepsy" are seriously affected by anoxia of even brief duration, whereas lower centers, less damaged by the same influence, allow survival to be maintained at a reflex or vegetative plane.

In the present experiment, pregnant bitches, whenever possible within the last week of pregnancy, were subjected to an atmosphere in which the oxygen content was lowered to as little as 4 per cent, for a period of from 20 to 30 minutes. Twenty-five pups, born from 24 to 72 hours after the experiment—the majority within the first 48 hours—died during the first few weeks. Three survived without apparent neurologic involvement. Those deaths which were investigated by necropsy revealed no cause for death. None suffered from distemper. Thus, it seems possible to state definitely that the pups which died shortly after birth did so because of the anoxia to which they had been subjected through their mothers.

Cases are reported of 2 pups which developed a convulsive state, one 5 and one 6 weeks after birth. It is felt that anoxia played a role in the development of this state.

The authors believe that a significant percentage of patients who suffer from convulsions for which no obvious cause can be ascribed have histories of complicated fetal life or birth. These comprise incidents that may be due to anoxia.

(The fetus has a very narrow margin of safety in respect to oxygen since, at best, its arterial blood is only about 65 per cent saturated with oxygen as compared with 96 per cent or better in the adult. At best, it exists in a continuous state of cyanosis. Under these circumstances, it is understandable that even a slight reduction in its oxygen supply may produce lethal damage. The practical inferences to be drawn from this fact in regard to obstetrical anesthesia are clear-cut; and it is hoped that this dramatic experimental demonstration by Fender, Neff and Binger of the deadly effects of fetal anoxia will be read and taken to heart by anesthetists everywhere.—Ed.)

disease is that couples be forewarned. It has been suggested that pregnancies be terminated before the end of the 10th lunar month but the helpfulness of this is doubtful since more infants die neonatally than are stillborn and one would have the further handicap of prematurity. The avoidance of any means of analgesia or anesthesia which is associated with a decreased oxygen-carrying capacity in the maternal blood is important. At present, the most important feature in the treatment of hemolytic disease is prompt transfusion of the infant with Rh-negative blood from a donor other than the mother. Red blood cell counts done on cord blood as soon as the infant is born should be routine on all infants of Rh-negative mothers. Oxygen therapy has proved to be of some assistance, particularly in the icteric and anemic groups of infants, and especially if the red blood count be markedly reduced.

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base of the lung was completely separated from the diaphragmatic dome. The mediastinum was pushed toward the left. The heart and the vascular pedicle were turned on their axis so that the usual relationships of the boundaries were not perceived at the same angle. Pleural pressure was taken by means of a Küss apparatus, +12, +7. Then 75 cc. of air were taken with a depression of 20 cc. of water, leaving the end pressure at -2, -4. The symptoms were relieved for one day but returned that evening with increasing vigor. The pleural pressure rose to +12, +8. Decompression of 125 cc. was made. There were no further signs of a return of the symptoms. An x-ray of the lungs made 12 days later showed no abnormalities nor sequelae of the pneumothorax.

(The possibility of spontaneous pneumothorax should always be borne in mind whenever a newborn infant shows persistence of dyspnea and cyanosis. The diagnosis will be made in most cases by fluoroscope or roentgenogram since the physical findings are not always clear-cut and may be misleading. I had a case of this condition a few years ago in which extraordinary dyspnea and cyanosis were present within 30 minutes after birth. An astute pediatrician made the diagnosis and, as was true in the case reported above, withdrawal of the air by needle resulted in a dramatic and permanent recovery.

There are several interesting aspects of this condition. The etiology is often obscure. Both in my own case and in that of Weill and Bourgin the infants breathed spontaneously at birth and no artificial respiration was used. The latter procedure, particularly forcible mouth-to-mouth insufflation, might well produce it. It seems to be much more common in males than in females; thus, in 17 cases reviewed by Glaser and Landau (*Am. J. Dis. Child.*, 50: 986, 1935), 11 were males, 4 were females and in 2 the sex was not stated. Both in my case and in the above French case, the infants were males. The condition is more commonly met on the left side, Glaser and Landau finding it on the left side in 11 cases, on the right in 4, bilateral in one and alternating in one. The prognosis of pneumothorax is believed to be somewhat better when it occurs in the neonatal period than when it develops later on, but it is always grave. Thus, Glaser and Landau found that 8 out of 17 neonatal infants died, or 47 per cent, whereas in a series of 300 cases of pneumothorax in older infants and in children up to 12 years of age, the mortality was 60 per cent.

Although withdrawal of the air with a needle and syringe is often successful, the relief may be only temporary and the procedure may have to be repeated one or more times.—Ed.)

SULFATHIAZOLE IN THE CONTROL OF EPIDEMIC DIARRHEA  
OF THE NEWBORN

MORRIS LEFF

Am. J. Obst. &amp; Gynec., 51: 87-89, 1946

The treatment usually employed in diarrhea of childhood is not sufficient to check epidemic diarrhea. The author has employed sulfathiazole with amazingly good results and considers it an almost specific remedy in this condition.

The drug must be given early and promptly to halt the disease before dehydration, great weight loss, acidosis and general metabolic upset have taken place. Nurses must be on the alert for frequent or watery stools and report the condition immediately. The stock solution used is made up of one grain sulfathiazole to the teaspoonful (0.06 Gm. to 4 cc.). The dose is repeated, one grain every 3 hours. It is given by medicine dropper or teaspoon directly into the baby's mouth. A few doses will usually control the diarrhea. Every baby in the nursery who has been exposed is given a prophylactic dose (one grain) of sulfathiazole.

It is concluded that sulfathiazole given promptly at the very onset of epidemic diarrhea in the newborn infant cures the disease in less than 24 hours and prevents its spread in the newborn nursery.

## A CASE OF SPONTANEOUS PNEUMOTHORAX OF THE NEWBORN

MARC-ADRIEN WEILL AND BOURGIN

Gynec. et obst., 44: 335-36, 1945

The authors report a case of spontaneous pneumothorax in a newborn infant. The course of pregnancy had been normal and no previous pathology had been noted in the family. Delivery took place normally after artificial rupture of the membranes. The infant's birth weight was 3500 grams and that of the placenta was 720 grams. The infant cried immediately after birth and progressed normally during the first 2 days of life with a weight loss of 35 grams. Because of the high fetal-placental relationship, he had been subjected to mercurial rubbings. Fifty-one hours after birth he exhibited slight expirational groaning, but cyanosis and movements of the alae nasi were absent and his temperature was normal. The next day (15 hours later) the groaning was accompanied by dyspnea and very marked cyanosis of the extremities. However, the temperature was normal and there were no signs of thoracic deformity, injury, rigidity or abnormal tension of the fontanelle. A radiograph was made to determine whether compressions of the thymic origin were present. This revealed a complete pneumothorax of the right hemithorax. The pulmonary stump was collapsed on its pedicle and the

The results in this case were entirely satisfactory. Unless another condition is present as a contraindication to the use of cyclopropane, this method seems to be applicable whenever laparotomy needs to be performed for a patient with respiratory paralysis.

(Both Dr. Rovenstine and Dr. Strauss are to be congratulated on the outcome of this case, in which seemingly insuperable obstacles were successfully overcome.—Ed.)

## CESAREAN SECTION ON A POLIOMYELITIC PATIENT CONFINED TO A RESPIRATOR

H. STRAUSS AND S. S. BLUESTONE

Am. J. Obst. & Gynec., 51: 114-20, 1946

A case is presented of pregnancy complicated by acute anterior poliomyelitis appearing in the 5th month and necessitating the continuous use of a respirator. The pregnancy was further complicated by acute pyelonephritis and acute diffuse glomerulonephritis. The progression of this nephropathy and the possibility of intrauterine fetal death required prompt action.

The authors believe that a patient with a quadriplegia plus almost total paralysis of all the muscles below the clavicles should be spared the added strain of labor. In this case, the patient was removed from the respirator and maintained with positive pressure to a rebreathing bag. An endotracheal airway was established and insufflation anesthesia with cyclopropane was administered while a classical cesarean section was performed. A healthy premature baby was delivered at the 35th week of gestation. The facilitation of chest expansion detected by the anesthetist upon removal of the baby was noted by the patient as she recovered from the anesthesia. Her condition improved following delivery and the only possible untoward effect of the respirator was prolonged, uncontrollable lactation. It was believed that the respirator played a large part in preventing distention. Delayed healing of the wound did not result.

Since the patient was constantly wet as a result of perspiration and incontinence, anhydrous calcium chloride was used in the respirator and is recommended to increase the comfort of respirator patients.

The authors believe that the method of management presented is applicable to all respirator cases requiring laparotomy.

## THERAPEUTIC ABORTION

I. A. SIEGEL AND S. G. KOHN

Bull. School Med. Univ. Maryland, 30: 125-29, 1946

The definition of therapeutic abortion as accepted by the authors is "the termination of an apparently normal intrauterine pregnancy before the period of viability in an effort to save or prolong the life of the mother." A review of the

## OPERATIVE OBSTETRICS

### THE ANESTHETIC MANAGEMENT OF PATIENTS WITH RESPIRATORY PARALYSIS REQUIRING LAPAROTOMY

E. A. ROVENSTINE AND H. STRAUSS

Am. J. Obst. & Gynec., 51: 213-16, 1946

The authors describe the anesthetic management of a patient with acute anterior poliomyelitis and respiratory paralysis who required cesarean section. The patient was 27 years of age and the pregnancy was further complicated by breech presentation and acute glomerulonephritis. The patient had overflow incontinence and was unable to defecate. All voluntary motor function of spinal innervation was lost except a very limited motion of the right hand. The cough reflex was absent and there was some facial paralysis. Any passive movement caused severe pain. Anesthesia was further complicated by prematurity (35 weeks' gestation).

In selecting the anesthetic agent, the existing nephropathy was considered reason for avoiding ether or chloroform. The desire to minimize postanesthetic nausea and emesis in a patient without a cough reflex added further reason for not employing volatile agents. The choice was then limited to the gases, the intravenous and the local agents with consideration to the one of these that could be adapted most conveniently to the technique required. Artificial respiration was essential during the entire time that the patient was outside the respirator and it was thought inadvisable to continue this any longer than necessary. Such techniques as local infiltration, regional nerve block and spinal were considered inadvisable because of the time required in using them. Inhalation anesthesia was favored to intravenous, since in the latter the drug must be eliminated by the body and effects on the fetus are still a subject of controversy. Since the convenience of cyclopropane administered during continuous artificial respiration is not surpassed by any other agent given by inhalation, it was the optimum choice.

Preanesthetic medication was not given in order to avoid any effects upon the fetus. Cyclopropane-oxygen was given by a mask and rebreathing bag which also served as a vehicle for continuous controlled respiration by manual pressure on the bag. An endotracheal airway was utilized. The stage of surgical anesthesia was obtained within 3 minutes and the baby was delivered 4 minutes after surgery had been started. The operation was completed in 25 minutes, at which time anesthesia was discontinued and the resuscitator put into use again. Four minutes later the patient was fully awake and rational.

Minute-to-minute determinations of blood pressure and pulse rate were made during the procedure. The blood pressure varied from 180/140 to 110/90; the pulse rate was 110 at the beginning of induction and remained rapid throughout. It was noted with interest that the pressure required to inflate the lungs became markedly reduced after the baby was delivered.

thoracoplasty was employed. Using standard suture scissors, a 2-inch incision was made parallel and close to the left costal border into the abdominal cavity. The first and middle fingers were slipped between the skin and the thoracic cage up to the axilla and then, working the scissors between the fingers, the ribs were divided up to the axilla. The hand was withdrawn, and when pressure was made on the chest, it collapsed enough to permit introducing the hand far enough to reach the anterior shoulder. With the assistance of a blunt hook, the anterior arm and shoulder were brought out and then the other shoulder was delivered. The head was delivered with Piper forceps. After delivery the fetus weighed 12 pounds,  $3\frac{1}{2}$  ounces, and the thorax resumed its normal contour.

The advantages of the procedure were: (1) facility of execution, about 5 minutes to complete delivery; (2) avoidance of mutilation of the fetus; and (3) the cut bones were completely covered by the undivided skin of the fetal thorax so that neither the maternal parts nor the hands of the operator were damaged.

literature reveals that the indications may be broad and may not confine to this definition. In this paper an analysis is presented of 80 cases of therapeutic abortion performed at the University Hospital from 1924 to 1943, inclusive. The incidence for all hospital admissions was one in 207 cases; for all out- and in-patients delivered it was one in 500 cases.

From a study of this series of 80 cases, it was found that some accepted indications for therapeutic abortion have been decreasing. For example, pulmonary tuberculosis, hyperemesis gravidarum, pyelitis and pyelonephritis, and cardiac disease, as a result of better understanding and treatment of these diseases, are decreasing as indications for therapeutic abortion. On the other hand, it was found that certain conditions still remain as important indications for termination of early pregnancy. These include all hypertensive conditions, with and without vascular and renal disease, premature separation of the placenta previa, acute hydramnios and fulminating preeclampsia.

Analysis of these cases shows that the principal indication for abortion was toxemic disease. Cardiac disease, not associated with cardiac failure, has never been an important indication. Not a single therapeutic abortion was performed on eugenic, social or economic grounds, although many sterilizations were done for these indications. Four maternal deaths resulted in this series; all took place in cases of hyperemesis gravidarum prior to 1935.

The choice of the vaginal or abdominal route for the termination of early pregnancy should depend upon the indication and whether or not sterilization of the patient is desirable, and upon those conditions which require prompt emptying of the uterus. The morbidity is greater in those cases terminated by the vaginal route, but not significantly higher than in those interrupted by the abdominal route.

(The decision as to whether therapeutic abortion is to be performed vaginally or abdominally should rest chiefly on the duration of the pregnancy. After the 12th week abortion from below becomes increasingly dangerous and abdominal hysterotomy is much preferable. Of course, as the authors point out, the desire to sterilize the patient may make the abdominal approach preferable even in pregnancies under 12 weeks. And let it be remembered that most conditions calling for therapeutic abortion call also for sterilization.—Ed.)

### SUBCUTANEOUS THORACOPLASTY ON THE PARTIALLY DELIVERED IMPACTED FETUS: A SUBSTITUTE FOR EMBRYOTOMY

CHARLES G. BARNUM

Am. J. Obst. & Gynec., 51: 282, 1946

A very large fetus was delivered by breech extraction to a point where the lower thorax was out but further progress could not be made. The fetus was dead. Rather than take the fetus apart to accomplish its removal, an adaptation of

by legislative act, an educational, research and service system of medical care which has stood the test of time and which is still progressing on all fronts. The quality of medical service depends upon the quality as well as the quantity of those who render it. The medical profession must be progressively maintained both qualitatively and quantitatively. Lastly, the rendering of high quality medical care depends not only upon personnel but also upon adequate facilities, which have never been available in all areas through no fault of the profession. Let the cooperative efforts of Federal, State and local resources provide the facilities, and private professional enterprise develop the personnel.

## SOCIAL AND LEGAL ASPECTS

### GOVERNMENT AND MATERNAL WELFARE

FRED L. ADAIR

Am. J. Obst. & Gynec., 50: 713-21, 1945

The fullness of life, the preservation of liberty and the attainment of happiness depend upon education and health. The function of a democracy is to assure freedom of opportunity to all to acquire the knowledge and health essential to their well-being. In our extensive country with its great variation in available resources and wealth as well as in concentration and diversity of population, there are manifold local problems which have to be solved largely by the intelligent interest of the local citizenry. These facts imply the development and establishment of some plan for the equalization of the distribution of wealth and personnel so that these essential opportunities may be available for all.

As the first consideration, namely, education, there are some serious gaps which need to be filled, many of which could be bridged by Federal, State or local governmental subsidies. In the matter of taxation, the equalization of monies to secure for each community the essential opportunities for health and knowledge should be accomplished with a minimum of centralized control and a maximum of local initiative and accomplishment.

Among the fields of health activities, that pertaining to maternity and infancy has great appeal. The Children's Bureau of the Department of Labor is a good example of the trend of the Federal Government in its health legislation and administration. The author presents a review of the activities of the Federal Government through this Bureau in an effort to show governmental trends by documentary evidence. The Children's Bureau has been the Federal agency which has been interested in the welfare and health of children and women. The quoted evidence shows that the original concept was not that which now constitutes its major activity, namely, a "Health Agency". Its activities have changed from investigation, advising and administration to supervision, administration and service. It is now concerned with women as well as infants and mothers. Primarily the programs have to do with health as distinguished from welfare.

As applied to individuals and communities, health is the result of carefully integrated comprehensive knowledge intelligently applied. The application begins with the individual and extends up through the family and the community to include progressively larger units of government.

Medical experts in their various fields have been the leaders and the Children's Bureau has been the medium. These men of science have been the product of the American system of medical education, investigation and practice. The present issue is whether governmental trends should be permitted to change seriously,

## TREATMENT WITH PENICILLIN OF SOME OBSTETRIC CASES

J. R. E. JAMES

J. Obst. &amp; Gynaec. Brit. Emp., 52: 501-05, 1945

The author's account of the use of penicillin presents illustrations of its value in cases of sepsis in obstetrics. The patients in this series consisted of 5 cases of Group A hemolytic streptococcal infections of the genital tract with complications and 2 cases of bullous impetigo in neonates. The 5 cases of streptococcal infection were first treated with sulfanilamide and penicillin treatment was started only when the infection proved uncontrolled by sulfanilamide.

The incidence of general peritonitis as a complication of streptococcal infections of the genital tract has been reduced by the sulfonamides. It remains to be seen whether or not penicillin, as illustrated in Case 1, will be a more effective form of treatment. In this particular case the initial course of penicillin was too short due to difficulty in obtaining penicillin at the time. In Case 2 general peritonitis had subsided but the onset of severe agranulocytosis with persisting heavy streptococcal infection provided the indication for penicillin. The patient made a satisfactory recovery after the initiation of penicillin therapy although she developed a superficial thrombophlebitis which gradually subsided. This is a not uncommon complication of penicillin therapy. The indication for penicillin in Case 3 was similar to that in Case 2. The patient made a rapid recovery. In Case 4, clinical response to sulfonamide therapy was not evident after 6 days, and on this indication penicillin was started with striking effect. In Case 5 it is suggested that parametritis, which followed a streptococcal genital tract infection, was due to a penicillin-sensitive organism, since the patient improved markedly on one week of penicillin therapy.

Two cases of staphylococcal bullous impetigo in neonatal infants responded well to penicillin ointment, the lesions being cleared within 6 days in one and 7 days in the other. In this respect, penicillin ointment, properly prepared and handled, offers a simple therapeutic measure worthy of further trial.

In the cases described the patients were very ill. The first 2 patients, in spite of early sulfonamide treatment, developed peritonitis. In Cases 2 and 3, sulfonamides were pushed to the stage at which agranulocytosis developed—a complication as dangerous as the original infection. Before penicillin was available, it is probable that Case 1, and possible that Cases 2 and 3, would have died. The rapid improvement with penicillin was therefore all the more striking.

The author concludes that these cases are few in number and it will be some time before the value of penicillin can be fully assessed and compared with that of the sulfonamides.

## MISCELLANEOUS

### PENICILLIN IN OBSTETRICS

H. A. POWER AND C. A. CRAVOTTA

Am. J. Obst. & Gynec., 51: 230-34, 1946

Penicillin apparently deserves serious consideration in obstetric complications attended by infection, potential or actual. The authors have reported a series of 45 patients treated with penicillin. The series included 9 patients with early acute mastitis, 6 patients subjected to cesarean section following complicated labors (penicillin was given prophylactically in these cases), 10 patients who had had cesarean section with clinical evidence of infection, 11 patients with postpartum infection, 5 septic abortions, 3 cases of known gonorrheal infection, one of pyelitis, one of pelvic cellulitis, 2 of thrombophlebitis and one of acute suppurative mastitis.

The results showed that acute mastitis responds with amazing rapidity and it is possible that lactation may be resumed. The prophylactic administration of penicillin following prolonged rupture of the membranes, prolonged inertial labors and in other patients potentially infected is apparently effective in assuring a smooth convalescence and in shortening the period of hospitalization. If this is substantiated by further investigation, it will undoubtedly broaden the use of low cesarean section. The authors advise that a routine culture should probably be taken from the lower uterine segment at operation. The treatment of infection following cesarean section in this series has been effective.

In incomplete septic abortion, particularly where there is a marked secondary anemia, a leucopenia, or both, penicillin is undoubtedly safer than the sulfonamides. The absence of other undesirable features of sulfonamide therapy will also recommend this drug.

Previously reported efficacy in the treatment of gonorrheal infection was substantiated by the results in the 3 cases reported herein. Penicillin therapy definitely improved the symptomatology in pyelitis. The authors' sole experience with postpartum pelvic cellulitis was disappointing; however, an occasional penicillin-resistant streptococcus or staphylococcus will undoubtedly be encountered, and may have been a factor in this case. No conclusions could be drawn from penicillin therapy and phlebitis.

Penicillin is apparently of value in the postoperative treatment of acute suppurative mastitis and may eliminate additional surgery. The disappearance of any vestige of induration was an outstanding finding in mastitis results in this group.

This small series, in which there were no mortalities and in which the hospital stay was of shorter duration than one would expect, warrants accumulation of additional data.

*Discussion:* The importance of keeping pregnant women under strict supervision from early in pregnancy until complete involution has taken place following delivery seems almost too elementary to warrant mention here. And yet, the failure on the part of the patient to seek or on the part of the attending physician to give adequate care during pregnancy is probably responsible for a majority of the fatalities associated with childbirth. Not only did the complete absence of prenatal care play a part in causing this death, but the gonococcal infection so closely following sexual intercourse leaves little doubt concerning the source of the organism which eventually killed the patient. Unfortunately this death occurred before the days of penicillin or streptomycin. It is possible that one of these magic bullets may have been more effectual than the sulfa drugs in saving this live.

## CASE NO. 13

The patient was a 15 year old colored primipara who registered at the prenatal clinic early in her pregnancy. Her prenatal course was normal until January 1 when her blood pressure was 144 mm. systolic and 96 mm. diastolic. At this time she was approximately 28 weeks pregnant. At her next regular visit two weeks later her blood pressure was 130/80, but on January 22 when she was again seen it was 142/92 and her urine contained 4 plus albumin. She was placed on a salt-free diet and told to return on January 29. During the next three days, however, she noticed a rapidly developing generalized edema. Because of the routine prenatal advice to report any swelling immediately, the patient went to the accident room of the hospital at 4:00 P.M. on January 25. She was promptly admitted to the hospital and upon examination, was found to be about 32 weeks pregnant, but the fetal heart could not be heard. The blood pressure was 160 mm. systolic over 104 mm. diastolic, the urine showed a 4 plus albumin, and there was a considerable amount of generalized edema. The heart and lungs were normal on examination. The hemoglobin was 85 per cent, the pulse rate 120 and the respirations 24 per minute.

At 5:00 P.M., one hour after coming to the accident room, she was given 250 cc. of 25 per cent glucose intravenously and 8 drams of paraldehyde by mouth. At 6:00 P.M. the blood pressure was 145/90. At 7:00 P.M. it had risen somewhat to 160/105, the pulse rate was 104 per minute and she was sleeping soundly. Another intravenous injection of 250 cc. of 25 per cent glucose was given at 9:30 P.M. At this time her pulse rate was 120, her respirations were 32 and she was becoming restless. At 9:45 P.M. she received 10 drams of paraldehyde per rectum. About 400 cc. of urine were obtained at this time by catheterization which showed a specific gravity of 1.005, a 3 plus albumin and no casts. The patient slept quietly following this paraldehyde and at 2:00 A.M. on January 26, another 250 cc. of 25 per cent glucose was given. At this time the blood pressure was 160/105. At about 3:30 A.M. another 8 drams of paraldehyde were given by rectum. For the next 7 hours her condition remained unchanged, the blood pressure varying from 160 to 180 mm. systolic and 95 to 110 mm. diastolic. At 10:00 A.M. 950 cc. of urine were obtained by catheter. The pulse rate was 112 and the respirations 34 per minute. She then began to develop noisy respirations. At 11:00 A.M. digitalization was begun. Because of the mucus in the trachea, catheter suction was attempted with some relief. At 12:00 noon the blood pressure was 130/90. The respirations gradually became more and more shallow and then suddenly ceased. Artificial respiration was started at once, oxygen was administered by mask, and coramine was given intravenously and intracardially. Respirations began again and soon the blood pressure returned to 160/90 and the pulse rate to 120 per minute. Five hundred cc. of plasma was given in the femoral vein. Oxygen was continued by mask with frequent tracheal suction to remove the accumulated mucus.

Shortly thereafter the patient's respirations ceased again but she was promptly revived

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# Maternal Mortality Reports

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*(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.*

*Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)*

## CASE NO. 12

The patient was a 31 year old colored multipara who was admitted to the hospital at 3:00 P.M. on January 31 with a history of ruptured membranes. In addition, she had passed a small amount of blood from the vagina. The patient was an unregistered one, having received no prenatal care. According to the history, the estimated date of confinement was in the early part of June. The patient's family and past history were non-contributory. There was no history of anything unusual until the morning of January 31. During the evening of January 30, however, the patient had sexual intercourse. At 4:00 A.M. on January 31 she began to have abdominal pains and shortly afterward, passed about a cupful of blood with some clots. At 10:00 A.M. her membranes ruptured spontaneously at home.

On admission to the hospital at 3:00 P.M. the patient had a temperature of 102.8 degrees F. by mouth. She did not appear to be acutely ill. The uterus was enlarged to about the size of a twenty-four weeks pregnancy and the uterus was contracting regularly. The head was engaged in the pelvis. The patient was typed and cross-matched and blood held in readiness if it was needed. There was only a very slight amount of bleeding after the patient entered the hospital, and it was felt that the patient would probably miscarry without any serious complications, although the elevation of temperature was considered a possible source of subsequent difficulties.

Labor pains continued throughout the evening and at 3:25 A.M. on February 1, the patient delivered a 28 week fetus weighing 2 pounds, 14 ounces which was stillborn. Three hours prior to delivery she had a rather severe chill following which her temperature rose to 103.8 degrees F. At this time a careful examination of the chest revealed no evidence of any abnormality and the urine was normal on examination. Following delivery, the temperature dropped to normal for 24 hours. This was followed by a second chill and the temperature this time rose to 104.8 degrees F. Blood cultures taken at this time were negative. The patient was started on sulfathiazole which she received at the rate of 90 grains daily for five days. At this time the history of intercourse 24 hours prior to delivery was obtained and the patient was changed over to sulfanilamide.

For the next 30 days the patient received 10 blood transfusions of 250 cc. each. Repeated blood cultures were negative until the 25th day following delivery when a culture taken at this time and several taken subsequently showed gonococci in the blood stream. At this time the patient was started on sulfapyradine intravenously. The lochia was foul throughout. At about the same time that the blood cultures were reported positive for gonococci, the patient developed an arthritis of the right shoulder joint. She became increasingly anemic in spite of the repeated blood transfusions. There were few localizing signs other than the endometritis and finally, on the 30th day post-partum, she died in spite of all therapy.

*Discussion:* The importance of keeping pregnant women under strict supervision from early in pregnancy until complete involution has taken place following delivery seems almost too elementary to warrant mention here. And yet, the failure on the part of the patient to seek or on the part of the attending physician to give adequate care during pregnancy is probably responsible for a majority of the fatalities associated with childbirth. Not only did the complete absence of prenatal care play a part in causing this death, but the gonococcal infection so closely following sexual intercourse leaves little doubt concerning the source of the organism which eventually killed the patient. Unfortunately this death occurred before the days of penicillin or streptomycin. It is possible that one of these magic bullets may have been more effectual than the sulfa drugs in saving this live.

## CASE NO. 13

The patient was a 15 year old colored primipara who registered at the prenatal clinic early in her pregnancy. Her prenatal course was normal until January 1 when her blood pressure was 144 mm. systolic and 96 mm. diastolic. At this time she was approximately 28 weeks pregnant. At her next regular visit two weeks later her blood pressure was 130/80, but on January 22 when she was again seen it was 142/92 and her urine contained 4 plus albumin. She was placed on a salt-free diet and told to return on January 29. During the next three days, however, she noticed a rapidly developing generalized edema. Because of the routine prenatal advice to report any swelling immediately, the patient went to the accident room of the hospital at 4:00 P.M. on January 25. She was promptly admitted to the hospital and upon examination, was found to be about 32 weeks pregnant, but the fetal heart could not be heard. The blood pressure was 160 mm. systolic over 104 mm. diastolic, the urine showed a 4 plus albumin, and there was a considerable amount of generalized edema. The heart and lungs were normal on examination. The hemoglobin was 85 per cent, the pulse rate 120 and the respirations 24 per minute.

At 5:00 P.M., one hour after coming to the accident room, she was given 250 cc. of 25 per cent glucose intravenously and 8 drams of paraldehyde by mouth. At 6:00 P.M. the blood pressure was 145/90. At 7:00 P.M. it had risen somewhat to 160/105, the pulse rate was 104 per minute and she was sleeping soundly. Another intravenous injection of 250 cc. of 25 per cent glucose was given at 9:30 P.M. At this time her pulse rate was 120, her respirations were 32 and she was becoming restless. At 9:45 P.M. she received 10 drams of paraldehyde per rectum. About 400 cc. of urine were obtained at this time by catheterization which showed a specific gravity of 1.005, a 3 plus albumin and no casts. The patient slept quietly following this paraldehyde and at 2:00 A.M. on January 26, another 250 cc. of 25 per cent glucose was given. At this time the blood pressure was 160/105. At about 3:30 A.M. another 8 drams of paraldehyde were given by rectum. For the next 7 hours her condition remained unchanged, the blood pressure varying from 160 to 180 mm. systolic and 95 to 110 mm. diastolic. At 10:00 A.M. 950 cc. of urine were obtained by catheter. The pulse rate was 112 and the respirations 34 per minute. She then began to develop noisy respirations. At 11:00 A.M. digitalization was begun. Because of the mucus in the trachea, catheter suction was attempted with some relief. At 12:00 noon the blood pressure was 130/90. The respirations gradually became more and more shallow and then suddenly ceased. Artificial respiration was started at once, oxygen was administered by mask, and coramine was given intravenously and intracardially. Respirations began again and soon the blood pressure returned to 160/90 and the pulse rate to 120 per minute. Five hundred cc. of plasma was given in the femoral vein. Oxygen was continued by mask with frequent tracheal suction to remove the accumulated mucus.

Shortly thereafter the patient's respirations ceased again but she was promptly revived

by means of artificial respiration. At 2:00 P.M. more glucose was given and because of her shallow respirations, carbon dioxide was added to the oxygen for a few minutes from time to time without much effect. At 2:45 P.M. respirations ceased for the third time, but this time, in spite of stimulation and efforts at artificial respiration including the use of a mechanical resuscitator, the patient was pronounced dead. A postmortem section was not done because at no time since admission had the fetal heart been heard. No autopsy was obtained.

*Discussion:* The occurrence of severe preeclampsia relatively early in pregnancy is rare. This case is one in which a patient with all the cardinal signs and symptoms of a toxemia including hypertension, edema and albuminuria, was sent home to await the onset of eclampsia. Strangely, this patient died without developing convulsions, and although no autopsy was obtained, the great likelihood is that she died of eclampsia. There are quite a few well authenticated cases of eclampsia without convulsions recorded in the literature. The case was called a preventable death because the patient was not hospitalized on January 22nd.

#### CASE NO. 14

The patient was a 19 year old primipara who was admitted to the hospital on April 23 at 9:00 A.M. in active labor. The personal and family histories were non-contributory. She was at term and the prenatal course had been uneventful until two weeks prior to admission when some elevation of blood pressure and edema were first noticed. The extent of the hypertension, weight gain and edema was not recorded.

On admission the blood pressure was 148 mm. systolic and 98 mm. diastolic and there was a moderate amount of ankle edema. Urinalysis was not done. The heart and lungs were normal on examination, the height of the fundus was 30 cm., the fetal heart was audible in the left lower quadrant, and the fetus in an L.O.P. position. On rectal examination the cervix was 4 cm. dilated and the presenting part at the level of the spines. Labor progressed without incident until 7:20 A.M. when the cervix was found to be fully dilated and the fetal head on the perineum. Prior to this, the blood pressure was 140/90 at 11:15 P.M. and 140/90 at 4:30 A.M.

Under nitrous oxide, oxygen and ether anesthesia, a lateral episiotomy was performed and a full term living female child weighing 6 pounds, 7 ounces, was delivered at 7:21 A.M. after a total labor of 42 hours and 21 minutes. She was delivered by her private physician and according to the notes made by the hospital intern on the patient's history, the third stage lasted five minutes, during which time vigorous Credé of the uterus was done associated with considerable pulling on the umbilical cord. The placenta and membranes were expressed intact accompanied by the loss of about 400 cc. of blood.

An ampule of ergotrate was given intravenously and another ampule intramuscularly. The episiotomy was repaired by 7:35 A.M. At this time the blood pressure was 95/55. The patient was returned to her room at 8:20 A.M. at which time no external bleeding was noticed. Ten minutes later, however, the pulse and blood pressure could not be obtained and the patient showed signs of marked shock. At 8:45 A.M. 500 cc. of 10 per cent glucose was started and at 9:10 A.M. morphine grains 1/6 was given. Nasal oxygen was started and at 9:20 A.M. plasma was begun.

The patient was seen by an obstetrical consultant at 9:30 A.M. She was in Trendelenburg position, her color was fair and she was able to answer questions rationally. However, her pulse was barely perceptible and her blood pressure was 60/35. Pressure on the fundus of the uterus caused the passage of several large clots of blood. The possibility of the existence of an inversion of the uterus was recognized and a sterile pelvic examination was decided upon. An ampule of pitocin was given by vein at 10:00 A.M. and an ampule of

ergotrate intramuscularly at 10:30 A.M. The blood pressure at this time was 70/55. At 10:45 A.M. the sterile pelvic examination was done under light anesthesia and the fundus of the uterus was found to be inverted and protruding through the cervical os for a distance of about two inches. Manual replacement was surprisingly easy. Following this, the uterus was tightly packed with wet gauze. The entire procedure took about 15 minutes. Between 11:00 A.M. and 12:00 noon, 500 cc. of whole blood was started. After receiving 100 cc. of this blood the patient had a severe chill and the blood was immediately discontinued.

At 1:00 P.M. the patient's temperature was 105 degrees F., her pulse was recorded for the first time since delivery at 180 per minute and the blood pressure was noted at 86/48. At 1:30 P.M. morphine sulfate grains  $\frac{1}{4}$  was given and by 2:00 P.M. the temperature was 106.8 degrees F., pulse rate 104, respirations 40 and blood pressure 84/68. At 2:30 P.M. adrenal cortex, coramine and ephedrine were given to the patient.

From this time throughout the night the patient remained in shock. Her temperature dropped to 102 degrees F., but at 6 A.M. the pulse was 168 per minute, she became quite cyanotic and, in spite of stimulants, she was pronounced dead at 7:30 A.M.

Postmortem examination showed the uterus to be large, soft and hoggy. There was a soft depression on the anterior surface of the fundus where the inversion had taken place. On opening the uterus, the area of insertion of the placenta was found to be in the fundus of the organ.

*Discussion:* Inversion of the uterus is not a rare complication of labor. When it occurs it is usually associated with a fundal insertion of the placenta, a lax uterine wall, too much pressure from above and traction on the cord. A properly conducted labor, with good management of the third stage, makes this accident a rare occurrence. This particular patient was quite badly handled in that a diagnosis was not made until several hours after she had gone into shock, she was ill-advisedly returned to her room too soon after her delivery which was associated with considerable bleeding, and to top it off, she developed a severe transfusion reaction which may have been more responsible for her death than anything else. Whether the blood was poorly matched or whether the Rh factor was involved here, one can only guess. This was called a preventable death.

#### CASE NO. 15

The patient was a 27 year old colored multipara who was admitted to the hospital on February 19. The personal and family histories were non-contributory. She had had two normal full term pregnancies prior to this conception, the last one eight years previously when her blood pressure averaged 120 mm. systolic and 80 mm. diastolic and her urine was negative for albumin and casts on repeated examinations. The last menstrual period was in August and the estimated date of confinement for this pregnancy was in May. There was no history of hypertension prior to this pregnancy and the prenatal course was reported as entirely uneventful until about two months prior to admission to the hospital when, according to the history given by her family physician, the blood pressure was 160/100 and there was some albumin in the urine. A temporizing course was followed despite continued high blood pressure.

On the morning of February 19 at 8:00 A.M. the patient complained of severe epigastric pains and vomited several times. Her physician was called and he prescribed some nembutal. At 2:45 P.M. on the same day the patient had a severe convulsion which was reported as lasting for 15 minutes and as being spastic in nature. She bit her tongue and lost control of her bowels and bladder. Her physician was again called and upon examination the patient was found to be unconscious and with a blood pressure of 260 mm. systolic and 110 mm. diastolic. She was immediately hospitalized.

Upon admission the patient was found to be in very poor condition. There was a considerable amount of generalized edema, she was comatose, and her respirations were slow and labored. The pulse was very weak and rapid and the blood pressure was 160/100. The skin was cold and clammy. The urine showed 4 plus albumin, many fine granular casts and white and red cells in great numbers. The heart sounds were weak and irregular and the lungs were filled with many coarse bronchial rales. The uterus was the size of a full term pregnancy and although the fetal head could be palpated above the symphysis, most of the uterus was hard and boardlike. She was bleeding only slightly by vagina. She was put in shock position and given 500 cc. of blood plasma. The blood pressure continued to be elevated and the fetal heart was inaudible. A diagnosis of abruptio placentae was made and the patient taken to the operating room for abdominal delivery. It was noticed on the operating table before the incision was made that there was some left-sided twitching of the extremities, the right side being flaccid. Sterile pelvic examination revealed a long, rigid cervix through which it was possible to palpate the fetal skull with one finger. The patient bled about 50 cc. of bright red blood as a result of this examination.

Under local infiltration anesthesia the peritoneal cavity was entered through a right rectus incision. Occasionally a small amount of nitrous oxide was supplemented to give necessary relaxation. The entire anterior surface of the uterus was deeply infiltrated with blood and presented the text book picture of the Convelaire uterus. A premature stillborn fetus weighing 4 pounds, 11 ounces, was removed from a uterus filled with many large new and old blood clots. On examination the posterior surface of the uterus was also found to be deeply discolored and there was considerable extensive hemorrhage in both broad ligaments. The uterus was removed and the abdomen closed. The patient received 1500 cc. of blood during the operation which she withstood remarkably well. Oxygen, digitalis and plasma and other fluids were given. On the second postoperative day, her intake was 2000 cc. and her output was 500 cc. There was a complete paralysis on the right side of the body including the face. Movements on the left side were normal. Both eye grounds showed large fresh hemorrhages in the macular region and elsewhere; the impression of the ophthalmologist was acute hypertensive retinitis. The blood pressure remained elevated, rising to 190/90 at times. She developed some evidences of pulmonary involvement with an elevation of temperature. Sulfa therapy, fluids and other supportive measures were given but the patient's condition grew rapidly worse and on the fourth postoperative day she died.

Autopsy revealed, among other findings, a cerebral subarachnoid hemorrhage, a cerebral hemorrhage of the left internal capsule and striatum, cloudy swelling and focal hemorrhages in the liver and bilateral confluent lobular pneumonia.

*Discussion:* Since this patient's expected date of confinement was not until May, the presence of hypertension in December (2 months before admission to the hospital and some five months before term) would place this patient in the category of chronic hypertensive vascular disease. In February pre-eclampsia became superimposed, then eclampsia and finally abruptio placentae.

The failure to hospitalize this patient in December for study and consideration of therapeutic abortion was an obvious error. Certainly, on hind sight, interruption of pregnancy would probably have saved this patient's life. The record of prenatal care between December and February is deficient, but it seems likely that evidence of developing pre-eclampsia could have been detected much earlier than it was, had the patient been carefully watched. The blatant blunder, of course, occurred on February 19th, when this desperately ill pre-eclamptic was passed by with the administration of a nembutal tablet,—an error which was tantamount to criminal neglect.

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# Gynecology

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## ENDOCRINOLOGY

### AN EVALUATION OF THE CLINICAL APPLICATIONS OF THE VAGINAL SMEAR METHOD

EPHRAIM SHORR

J. Mt. Sinai Hosp., 12: 667-88, 1945

The author reviews in this paper the results of studies made to determine the possible usefulness of the vaginal smear technic introduced by Papanicolaou as a method for evaluating both normal and pathological ovarian function and as a guide to therapy. As might be expected, the method was found to share certain limitations with all other present methods of observing ovarian function; hence, it is most ideally used in conjunction with other procedures such as urinary hormonal assays and endometrial biopsies. However, when used as a sole method of study, with consideration of its limitations, it can serve as an extremely satisfactory picture of ovarian function and serve as a sensitive guide for the most efficient use of the therapeutic agents now available.

The proper use of this method is dependent upon adequate fixation of the secretions and the utilization of specific staining methods capable of revealing cellular detail. It is essential to fix the slide while the secretion is moist since drying alters the staining reaction sufficiently to make the interpretation of the smear unreliable. The smears may be stained with a variety of methods. The following single differential stain has proved extremely satisfactory for office use:

Ethyl alcohol (50%).....	100 cc.
Biebrich Scarlet (water sol.).....	0.3 gm.
Orange G.....	0.100 gm.
Aniline blue (water sol.).....	0.025 gm.
Fast Green FCF.....	0.075 gm.
Phosphotungstic acid, c.p.....	0.25 gm.
Phosphomolybdic acid, c.p.....	0.25 gm.
Glacial acetic acid.....	1.0 cc.

The basis for the use of the vaginal smear as a method for studying ovarian function may be stated briefly in the following manner. The vaginal epithelium possesses a 3-zone structure which alters in characteristic fashion with the changing pattern of the ovarian hormones elaborated during the menstrual cycle. These changes are reflected in the cells which are constantly shed into the vaginal cavity. In this way, the cytological changes specifically due to the estrogenic

hormones can be recognized both with respect to the structure of the vaginal epithelium and the vaginal secretion.

In evaluating the vaginal smear picture, one should systematically make a note of the following characteristics:

1. The size and shape of the epithelial cells and their staining properties.
2. The size and shape of the nuclei and the details of their structure.
3. The extent of cellular desquamation.
4. The distribution of the cells whether discrete or in clumps.
5. The amount and character of the accompanying mucus.
6. The extent and character of the leucocytosis.
7. The degree of cellular destruction as indicated by free nuclei.
8. The presence of endometrial cells.
9. The presence of red cells, either well preserved or shadow forms, and fibrin.
10. The bacterial content.

Factors complicating the interpretation of the smear should be born in mind, such as cervical erosions, endocervicitis and trichomonas.

Evaluation of the normality of menstrual cycles may be facilitated by the collection of a series of slides covering a whole menstrual cycle from patients of proved fertility. The writer favors the following system of dividing the menstrual cycle into its significant episodes:

A. The menstrual phase—this is the breakdown phase during which desquamation usually involves the entire functionalis and part of the intermediate zone. This generally lasts 4-5 days.

B. The postmenstrual phase (5-8 days)—during which there is a gradual change in the epithelium and vaginal smear under the influence of the growing follicle.

C. The preovulatory phase (2-3 days)—this is characterized by a sudden spurt of estrogenic activity accompanied in the smear by striking and usually progressive increase in the percentage of cornified cells and a gradual clearing of the smear.

D. The ovulatory peak (generally 1 day)—which is the expression of the height of follicular development just prior to ovulation. The secretion is thin, clear and leucopenic. There is a predominance of thin, wafer-like cornified cells with small, pyknotic nuclei.

E. The postovulatory reaction (generally 1 day)—this is the surest available guide for determining the time of ovulation. The better the cycle the sharper are the cytological changes, which consist of leucocytosis, clumping, folding and curling of the cells, and generally, a reduction in the cornified elements.

F. The luteal phase (10-14 days)—may be divided into early luteal phase lasting 3-4 days during which considerable cornification is likely to persist due to the shedding of the upper cornified layers previously built up under the influence of the estrogenic hormone; and late luteal phase which is the expression of the increased growth and desquamation of the luteal epithelium resulting from the combined action of estrogen and progesterone. The cells are abundant and are usually present in thick clumps imbedded in a thick mucoid secretion. Corni-

fied cells are significantly reduced in number and non-cornified cells show small nuclei predominating. Frequently they show a characteristic type of folding.

G. Premenstrual phase (1-3 days)—this smear is a reflection of the waning hormonal production and is generally thinner and less rich in cells. There may be a moderate increase in cornified cells and erythrocytes may be present.

Figure 1 illustrates the cytological changes occurring in the menstrual cycle of a patient of proved fertility.

By means of serial studies of the vaginal secretion it has been possible to recognize at least 4 distinct types of amenorrhea. They are as follows:

A. *The atrophic, acyclic type*: This is characterized by a uniformly atrophic smear in which the predominance of deep cells indicates virtual absence of estro-

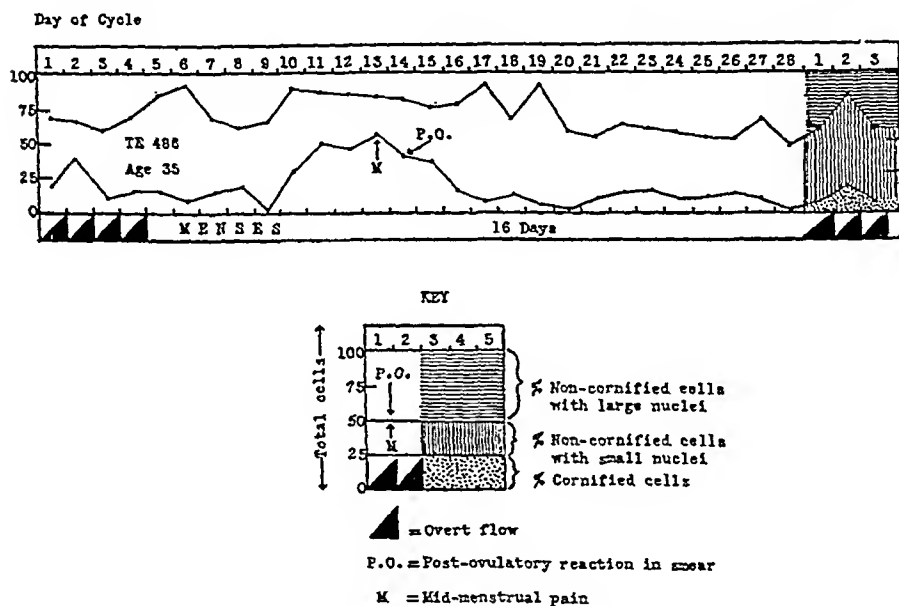


FIG. 1. Changes in the vaginal smear picture during a normal ovulatory cycle

genic hormone production. This type of smear is seen in many cases of "primary" amenorrhea and also occurs in "secondary" amenorrhea.

B. *The subfunctional acyclic type*: Here a variety of vaginal smear pictures is exhibited having, however, 2 common characteristics; they do not vary significantly from day to day, and they all reveal appreciable ovarian insufficiency. The cells are more developed than in the atrophic smear. Cornified cells are absent or rare. This type of smear is characteristically seen in "secondary" amenorrhea.

C. *The subfunctional cyclic type*: This group presents a fluctuating type of vaginal smear picture with recurring episodes of cyclic ovarian activity resulting in significant estrogenic hormone production and a high degree of cornification.

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Androgenic hormones have a 2-fold action; in proper concentrations they can neutralize the peripheral effects of the estrogens on the endometrium and vaginal epithelium, and their 2nd effect is the suppression of the gonadotrophic activity of the pituitary. Both of these effects are of practical importance in the management of certain menstrual disorders and the use of these hormones is most efficiently controlled by vaginal smear studies.

(It is possible that I am wrong, but I have the impression that enthusiasm for vaginal smear study as a practical diagnostic aid in gynecological practice is definitely less than it was some years ago. In spite of Shorr's insistence on the simplicity of the method, its intelligent use except perhaps as an index of estrogenic activity, implies a degree of cytological knowledge which few practicing gynecologists possess. Even the enthusiasts are willing to concede its very great limitations as an index of progesterone activity. It was at first urged by the enthusiasts that vaginal smear study should serve as a guide to estrogenic therapy in the menopausal syndrome, but it appears to have been definitely established that the vasomotor symptoms do not necessarily parallel the estrogen changes in the vagina, and that such symptoms often disappear before estrogen therapy brings about any great degree of cornification, just as they often disappear long before urinary titre shows any great drop in the urinary gonadotrophes. The vasomotor symptoms themselves, and not the vaginal changes, should be the target of therapy. This is a very inadequate discussion of the whole question, and it is easy to see that I am something of a reactionary on this point. Personally I believe that endometrial biopsy, usually exceedingly simple from a technical standpoint, and far simpler and more satisfactory from the standpoint of microscopic evaluation, is a much better method for the study of ovarian hormonal function.—Ed.)

## MENSTRUAL DISORDERS IN HYPERTHYROIDISM

GUILLERMO DI PAOLA, O. SINISCALCO AND A. CASANOVA

Bol. Soc. de obst. y ginec. de Buenos Aires, 26: 129-38, 1945.

For a long time it has been known that therapeutic administration of thyroid stimulates ovarian function. According to Arrighi's late experimental work, it is possible that small doses of thyroid stimulate the ovaries, while larger ones administered for a long period of time might depress ovarian activity.

Most authors are inclined to believe that this thyro-ovarian relationship is maintained through the metabolic activity of the thyroid gland.

In a statistical study the authors report the incidence and type of menstrual disorders observed in 82 patients presenting hyperthyroidism or thyrotoxicosis, which they were able to follow up. These cases were divided into the following groups: (1) Exophthalmic goiter (49 cases); (2) Toxic adenoma (19 cases; and (3) Hyperthyroidism without goiter (14 cases). According to the severity of the symptoms, the cases were classified into slight hyperthyroidism (B.M.R. below plus 30), medium (B.M.R. between plus 30 and 50) and severe (B.M.R. above plus 50).

Analysis of this study showed that 60 per cent of the cases did not show any

These episodes may occur at fairly regular intervals or may be widely spaced. This type of amenorrhea is, with few exceptions, limited to the "secondary" group.

D. *The hyperfunctional acyclic type*: This is the least common type and, in the author's experience, has been confined to the "secondary" amenorrhoeas. The vaginal smear shows a significant degree of cornification with no luteal transitions throughout the period of amenorrhea.

This classification of amenorrhoeas by vaginal smear types can, either alone, or supplemented by urinary gonadotrophic hormone assays, provide a valuable guide to therapy. Therapeutic measures are of 3 types: (1) general or correctional; (2) stimulative; and (3) substitutional. When general or correctional measures are employed, their effects on ovarian function can readily be evaluated by the vaginal smear. Stimulative therapy with gonadotrophins is admittedly unreliable. One factor responsible for some failures may be the absence of adequate criteria for estimating individual requirements. Such uncertainty can be resolved by the aid of the vaginal smear. At present, substitutional therapy is more generally employed for the management of amenorrhea. This consists in the cyclic administrations of estrogens alone or in combination with progesterone. In certain cases, the vaginal smear can provide information as regards the administration of substitutional therapy.

One of the earliest applications of the vaginal smear method was its use in the management of the menopausal syndrome. The prevailing vaginal smear types at the menopause indicate the presence of significant ovarian insufficiency. The administration of adequate amounts of estrogen transforms the smear to the estrus type, with the amelioration of menopausal symptoms. The vaginal smear changes which thus occur are among the simplest from the histological point of view and should present little difficulty in evaluation.

The utilization of the vaginal smear method in the management of infertility and the menometrorrhagias requires more experience than is necessary for its use in the menopause and in amenorrhea. In studying vaginal smears for infertility of functional origin, 3 types of anovulatory cycles are most frequently encountered. The first is characterized by a uniform vaginal smear picture throughout the cycle with cytological characteristics indicative of gross ovarian insufficiency. The 2nd type simulates the picture seen in an atrophic acyclic amenorrhoeic subject. The 3rd variety of anovulatory cycle is marked by a persistently high degree of cornification throughout the cycle with no signs of postovulatory reaction or luteal phase. When infertility is due to the male partner and artificial insemination is used, the vaginal smear can aid in determining the appropriate time for the procedure and reduce the number of inseminations necessary.

Meno- and metrorrhagia present some of the most difficult problems both in diagnosis and management. The most reliable present form of treatment consists of the premenstrual induction of a well developed secretory endometrium by the administration of adequate amounts of progesterone and the interruption of therapy 2 to 3 days before the expected flow. The effects of progesterone are readily recognized in the vaginal smear.

dometriosis has been *successfully* treated by castration. The clinical impression exists that oral estrogens increase the pain of residual endometriosis. The following case is presented because the patient showed a more objective symptom than pain.

The patient, a 36 year old woman, was first seen with the complaint of tarry stools. Bleeding from the bowel had begun 3 years previously, since which time all investigations as to the source of bleeding had been fruitless. She was given repeated transfusions and an operation was performed. No cause for the bleeding was found in the upper gastrointestinal tract. The patient was readmitted several times, requiring many transfusions and a second exploratory laparotomy was performed without positive findings. Proctoscopy was repeatedly negative.

It was then noticed that the bleeding episodes corresponded to the time of the menstrual periods and, after gynecologic consultation, an operation again was performed. Small areas of endometriosis were found high on the rectum. Both ovaries and the uterus were removed.

The patient was well until menopausal symptoms occurred and diethylstilbestrol was given. After a few days of this therapy, she fainted, vomited and was readmitted with rectal bleeding. She was transfused and the stilbestrol therapy was discontinued. Permanent recovery has followed the discontinuance of this therapy, the menopausal symptoms being fairly well controlled by sedatives.

(The opening sentence of this paper states that removal of both ovaries *usually* stops the progress of endometriosis, implying that there are exceptions to this sequence. A few have been reported, but always one doubts whether some ovarian tissues have not remained behind in the patient, either in the pelvis or elsewhere, simply because such an occurrence is so contrary to universal experience as well as to what we know about the dependence of endometrial growth upon ovarian function. A great many years ago the British gynecologist, Doran, reported a case in which menstruation persisted after complete removal of both ovaries. Some years later, however, he was spunky enough to report that this patient was later delivered of a baby, which is pretty good proof that some ovarian tissue was still present. It is conceivable, perhaps, that some extra-ovarian source of estrogen, such as the adrenal cortex, might keep up the growth of residual endometriosis, as it appears at times to cause postmenopausal activity in the uterine mucosa itself. To my mind, this would be a more plausible explanation than to speculate that the growth characteristics of the endometrium "become irreversible".

However, one can logically expect that the administration of estrogens would reactivate, though only temporarily, endometrial lesions wherever they may be, as in the case reported by Faulkner and Riemenschneider. If a woman is castrated at the age of 20, for example, and estrogenic therapy in sufficient dosage be given at the age of 90, it should be possible to produce striking proliferation of the endometrium. For that matter, if the estrogen is followed in proper sequence and dosage by progesterone, a perfect simulation of a menstrual histological cycle can be produced, and exactly this type of clinical experiment has been reported by Clauherg and others.

When a woman is left with a residual endometriosis in the pelvis, estrogen therapy for postmenopausal symptoms should be used sparingly and interruptedly, or perhaps better not at all, testosterone being substituted. Where the residual tissue is located in the intestinal wall, in which location reactivation might mean external hemorrhage, the contraindication to estrogen therapy is all the greater.—Ed.)

menstrual irregularity. Menstrual disorders were observed in the remaining 40 per cent, much more frequently in the group of severe thyrotoxicosis, which included by far the largest number of cases (61 per cent), and mainly in patients with toxic adenoma.

The menstrual disorders were chiefly hypomenorrhea (60 per cent) and amenorrhea (22 per cent). The simple finding of hypomenorrhea, however, does not necessarily indicate ovarian insufficiency—except when it precedes amenorrhea—since other causes, such as endometrial or vascular conditions, may be responsible for it. When amenorrhea appears as the first symptom of thyrotoxicosis, it may be due to the same neuro-psychic factor which caused the latter.

The menstrual disorders in hyperthyroidism progress according to the nutritional state and metabolic changes of the patient.

As a matter of fact, in the cases which underwent operation (thyroidectomy) almost always an improvement or cure of the menstrual disturbances was noted.

The results of this statistical study do not agree with the classical concept which admits the incidence of menstrual irregularities in the majority of women with hyperthyroidism, although they do prove the well known fact that menstrual disorders occur more frequently in the severe forms of the disease.

(This study appears in general to bear out the dictum laid down many years ago by Hertoghe that hyperthyroidism is more likely to bring about scantiness or absence of menstruation than excess of the flow, while the reverse is true of hypothyroidism. However, there are many individual exceptions to this general rule. For example, hypothyroidism is certainly to be found in some, though not the majority of cases of endocrinopathic amenorrhea. As a matter of fact, we know very little as to the interrelations between the thyroids and the gonads, though everyone, certainly practically every clinician, believes them to be important. Nor do we know whether this relation is a direct one between the two endocrine glands or whether it is mediated through the pituitary, as is more likely. Thyroid therapy in functional gynecological disorders is most often on an empirical basis. It is curious, and rather amusing, that this empiric therapy probably yields more frequently satisfactory results than the employment of ovarian and gonadotropic substances for the attempted correction of aberrations in the reproductive endocrinology concerning which we think we have learned so much.—Ed.)

## REACTIVATION OF ENDOMETRIOSIS BY STILBESTROL THERAPY

R. L. FAULKNER AND E. A. RIEMENSCHNEIDER

Am. J. Obst. & Gynec., 50: 560-61, 1945

Removal of both ovaries *usually* stops the progress of endometriosis and results in recession of residual lesions not removed at operation. In certain instances growth characteristics of the lesions apparently become irreversible before operation is performed. However, some interest attaches to the question of ovarian hormonal therapy for menopausal symptoms in patients in whom en-

sufficiently large doses of any estrogen—in functional bleeding. As Bickers says, this would apply more particularly to the common “anovulatory” type.

Making use of this primarily effective action of large estrogen dosage in the immediate control of bleeding, various other investigators, especially Hamblen, have developed rather elaborate plans of so-called cyclic therapy, employing both estrogens and progesterone, according to the schedule described in Bickers' paper. While the results, at least in my own hands, have not been nearly as infallible as would appear from some reports, and while simpler and less expensive plans give satisfactory results in perhaps the majority of cases seen clinically, this cyclic plan should certainly be a part of the gynecologist's armamentarium in the difficult and distressing problem of treatment of the more severe cases.—Ed.)

## ORAL THERAPY WITH ETHINYL ESTRADIOL IN THE MENOPAUSE

H. WIESBADER AND W. FILLER

*Am. J. Obst. & Gynec.*, 51: 75-81, 1946

A series of 53 women with menopausal symptoms was treated with ethinyl estradiol. All were satisfactorily relieved 6 to 9 days after institution of therapy. The initial treatment plan, which called for 0.05 mg. of ethinyl estradiol 3 times daily, was abandoned since side effects occurred in 6 patients. By reducing the daily dose to 0.05 mg., gastrointestinal disturbance could be eliminated completely. Consequently, the initial daily dose in all patients was changed to 0.05 mg. This dose was tolerated well without exception and could be increased with impunity. The optimal therapeutic amount was given for 3 to 4 weeks after which the daily dose was reduced to a maintenance level.

Repeated vaginal smear studies were carried out in all cases. Preliminary vaginal smears in the majority of instances revealed marked estrogen deficiency. Smears studied when patients were changed to the maintenance dose usually showed good cornifications. However, not in all cases did the smear picture parallel the subjective response. Premedication endometrial studies of 10 patients revealed an atrophic endometrium in 5 instances and some degree of proliferation in the other 5. Specimens taken between 14 and 20 days after initiation of therapy showed a cystic and glandular hyperplasia in one instance and good proliferation in all others. Preliminary urinary prolans were present and estrogenic hormones absent in 10 cases investigated.

Clinical results of other investigators with ethinyl estradiol in climacteric patients are discussed. It is concluded that the new hormone is very effective when administered by mouth. There is complete absence of side reactions if minimal effective doses are administered. 2 figures.

(Since it is unquestionably an effective estrogen, it is not surprising that ethinyl estradiol, like many other estrogenic products, hormonal or non-hormonal, gave such satisfactory treatment in this group of menopausal cases. By the same token, it may be taken as for granted that any good estrogenic preparation on the market today—and the Biological

## ETHINYL ESTRADIOL IN THE TREATMENT OF METRORRHAGIA

WILLIAM BICKERS

Am. J. Obst. &amp; Gynec., 51: 100-03, 1946

Approximately  $\frac{1}{2}$  of the patients seen in private practice with acyclic bleeding from the uterus have an organic basis for that bleeding. The other half bleeds from the uterus as a result of abnormal physiology in the pituitary-ovarian endometrium cycle. The latter group must be subdivided into 2 groups: (1) those who bleed from a secretory phase endometrium and who are essentially normal endocrinologically, and (2) the patients in whom the bleeding comes from a proliferative phase endometrium. The second group are candidates for treatment by endocrine therapy.

A series of 12 patients suffering from anovulatory metrorrhagia were treated with ethinyl estradiol, 0.3 mg. administered daily for 20 days. Progesterone (5 mg.) was administered daily by hypodermic injection on the last 5 days of ethinyl estradiol administration. Uterine bleeding stopped in all cases except one within 6 days after starting treatment. When the ethinyl estradiol-progesterone 20-day treatment was stopped, all patients menstruated within 5 days. On the 5th day from the onset of this induced bleeding episode, the 20-day treatment was resumed and another bleeding episode occurred in all patients within 5 days after completing the 2nd cycle of treatment. A 3rd cycle of treatment was administered in the same manner. Follow-ups were made from 3 to 12 months after treatment.

It is concluded that ethinyl estradiol in oral dose of 0.3 mg. is comparable to diethylstilbestrol in oral dose of 5 mg. in so far as control of anovulatory bleeding is concerned. The incidence of regular cyclic bleeding following both types of treatment is about the same. However, the ovulation salvage in the ethinyl estradiol group (35 per cent) was distinctly better than that in the diethylstilbestrol treated group (16 per cent).

(It is a curious thing to note the change of opinion and practice which has occurred in recent years as regards the role of estrogens in the treatment of functional uterine bleeding, more particularly the group diseased by Bickers, corresponding to that designated by Schröder as metropathia hemorrhagica. The oversimplified explanation of the mechanism of such bleeding has been that it is due to a relative excess or persistence of estrogen and an absence of progesterone. It seemed wrong to give estrogen to correct such a mechanism, and the more common methods of treatment were directed to the administration of the lacking progesterone or the lessening of the estrogen excess through the administration of testosterone. It was commonly accepted that the bleeding phases were due to drops in the estrogen level, and while these might be prevented by propping up the endometrium with estrogens in rather large doses, this method was looked upon as an unsatisfactory stop-gap. Certainly for the prompt cessation of long continued bleeding, the administration of large doses of such estrogens as stilbestrol is far more effective than any other hormonal measure. Although it may not be indelicate to say that he has been severely criticized by many for over-enthusiasm for stilbestrol therapy in general, Karnaky deserves the credit for emphasizing the rather promptly hemostatic effects of stilbestrol—and the same would apply to

state he has found them 35 times among 79 biopsies; in the estrin-lutein state, 62 times among 77 biopsies. In 6 of the last group, the absence of spiral arterioles can be explained by the smallness of the biopsy fragment.

The spiral arterioles can, in certain instances, present qualitative histological modifications. The thickening of fibro-elastic perivascular matter is frequently accompanied by a fibrous reaction of the chorion. This state exists nearly always in intermediary follicular states.

Deciduiform transformation is characterized by a modification of the chorionic cells which augment in size and fill with glycogen. This state has been brought about by injection of large doses of progesterone. The author has never found this state of deciduiform transformation in the intermediary follicular state. He has seen it in 17 out of 77 cases of the estrin-lutein state.

In conclusion, it can be said that the development and growth of spiral arterioles is secondary to the activity of the corpus luteum and to the action of progesterone associated with that of estradiol. It seems logical to allow that the estrogens alone are incapable of producing the differentiation of spiral arterioles; this information may be important from the point of view of cytohormonal exploration.

## GROWTH OF CORPUS LUTEUM IN RATS DURING PREGNANCY AND FOLLOWING INJECTIONS OF TESTOSTERONE

G. L. LAQUER AND P. KOETS

Proc. Soc. Exper. Biol. & Med., 60: 239-45, 1945

A total of 306 female rats belonging to the Stanford strain of albino rats were used in this study. Only those rats with vaginal estrus cycles of 4 to 6 days were used. The ages of the animals varied from 90 to 150 days. Control values were obtained from 65 rats which were killed within 24 hours after the disappearance of vaginal estrus. Eighty-two rats were used for the analysis of corpora lutea during pregnancy. To 118 rats testosterone propionate was given subcutaneously, the initial treatment being given during late estrus after cornified cells had been present in the smear for at least 15 hours. Two dosage levels were used; some of the rats received 0.5 mg. daily and others received 2.5 mg. daily.

The 3 weight curves of corpus luteum in pregnant rats, in rats receiving 0.5 mg. testosterone propionate and in rats receiving 2.5 mg. are essentially the same, indicating that the corpus luteum grows in the same fashion during periods of testosterone injections as it does during the course of pregnancy.

It is observed that the total lipids in the pregnant rat show a slight decrease during the first 16 days followed by a marked rise at the 18th day of pregnancy. About 2 days following littering there is a drop in total lipids which lasts a few days and is followed by a second rise.

Division of the Federal Pure Food and Drug Bureau reports that practically every estrogenic preparation on the market actually has the estrogenic content and potency represented by its label—will have the characteristic estrogenic proliferative effect upon the vaginal mucosa, the endometrium and the urinary hormones.

For practical purposes, therefore, there is no need to control therapy with vaginal smears or urinary hormone titres as was done in the present study, interesting though these may be. This is especially true since such studies often show a lack of parallelism with the clinical results, as the authors themselves found, and as many previous investigators have reported. The practical target for therapy, more trustworthy than vaginal smears or urinary studies, is furnished by the vasomotor symptoms themselves, but certainly not by such symptoms as nervousness, irritability and headaches. In the absence of the actual hormone-withdrawal vasomotor symptoms, these more indefinite middle-age manifestations are rarely menopausal, and will not be helped by the injudicious administration of estrogens. I feel very strongly that estrogens should be used only when and if the vasomotor symptoms are really troublesome, that the doctrine of fixed or maintenance dosage is a pernicious one, and that the "prophylactic" use of estrogens advocated by some is illogical and possibly harmful. Moreover, by keeping up a sort of substitutional ovarian function, I believe that the prolonged use of so-called maintenance doses may actually prolong the duration of the menopause. However, I have elaborated on these points previously and will undoubtedly have occasion to comment on them in the future.—Ed.)

## MODIFICATIONS IN THE SPIRAL ARTERIOLES OF THE UTERINE MUCOSA IN THE LIGHT OF CYTOHORMONAL EXPLORATION

A. LIESSE

Gynéc. et obst., 44: 223-25, 1945

The physiological problem of menstruation is not only hormonal but it admits a local vascular determinism. Others have emphasized the importance of the problem of vascular physiology laid down by menstrual hemorrhage. Certain writers have shown secondary vascular modifications with the intrauterine instillation of zinc chloride. It seemed of interest to the author to undertake a systematic study of the frequency of spiral arterioles in the 100 latest endometrial biopsies at the gynecological clinic.

The vascularization of the uterine mucosa is composed of 2 types of arteries: (1) arterioles of long course, called spiral; and (2) arteries of short course which do not extend beyond the basal or compact layer of the mucosa. The spiral arterioles present modifications in the course of the genital cycle; the second group does not present very characteristic ones.

It is known that, following the action of progesterone, the conjunctival spines distort the wall with glandular tubules (estrin-lutein state). When the conjunctival spines are well formed, one nearly always finds well differentiated spiral arterioles.

The present systematic study of spiral arterioles has been made at different stages of development of the uterine mucosa. The author has never encountered spiral arterioles in the follicular state of the mucosa; in the intermediary follicular

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A. LIESSE

Gynéc. et obst., 44: 223-25, 1945

The physiological problem of menstruation is not only hormonal but it admits a local vascular determinism. Others have emphasized the importance of the problem of vascular physiology laid down by menstrual hemorrhage. Certain writers have shown secondary vascular modifications with the intrauterine instillation of zinc chloride. It seemed of interest to the author to undertake a systematic study of the frequency of spiral arterioles in the 100 latest endometrial biopsies at the gynecological clinic.

The vascularization of the uterine mucosa is composed of 2 types of arteries: (1) arterioles of long course, called spiral; and (2) arteries of short course which do not extend beyond the basal or compact layer of the mucosa. The spiral arterioles present modifications in the course of the genital cycle; the second group does not present very characteristic ones.

It is known that, following the action of progesterone, the conjunctival spines distort the wall with glandular tubules (estrin-lutein state). When the conjunctival spines are well formed, one nearly always finds well differentiated spiral arterioles.

The present systematic study of spiral arterioles has been made at different stages of development of the uterine mucosa. The author has never encountered spiral arterioles in the follicular state of the mucosa; in the intermediary follicular

state he has found them 35 times among 79 biopsies; in the estrin-lutein state, 62 times among 77 biopsies. In 6 of the last group, the absence of spiral arterioles can be explained by the smallness of the biopsy fragment.

The spiral arterioles can, in certain instances, present qualitative histological modifications. The thickening of fibro-elastic perivascular matter is frequently accompanied by a fibrous reaction of the chorion. This state exists nearly always in intermediary follicular states.

Deciduiform transformation is characterized by a modification of the chorionic cells which augment in size and fill with glycogen. This state has been brought about by injection of large doses of progesterone. The author has never found this state of deciduiform transformation in the intermediary follicular state. He has seen it in 17 out of 77 cases of the estrin-lutein state.

In conclusion, it can be said that the development and growth of spiral arterioles is secondary to the activity of the corpus luteum and to the action of progesterone associated with that of estradiol. It seems logical to allow that the estrogens alone are incapable of producing the differentiation of spiral arterioles; this information may be important from the point of view of cytohormonal exploration.

## GROWTH OF CORPUS LUTEUM IN RATS DURING PREGNANCY AND FOLLOWING INJECTIONS OF TESTOSTERONE

G. L. LAQUER AND P. KOETS

Proc. Soc. Exper. Biol. & Med., 60: 239-45, 1945

A total of 306 female rats belonging to the Stanford strain of albino rats were used in this study. Only those rats with vaginal estrus cycles of 4 to 6 days were used. The ages of the animals varied from 90 to 150 days. Control values were obtained from 65 rats which were killed within 24 hours after the disappearance of vaginal estrus. Eighty-two rats were used for the analysis of corpora lutea during pregnancy. To 118 rats testosterone propionate was given subcutaneously, the initial treatment being given during late estrus after cornified cells had been present in the smear for at least 15 hours. Two dosage levels were used; some of the rats received 0.5 mg. daily and others received 2.5 mg. daily.

The 3 weight curves of corpus luteum in pregnant rats, in rats receiving 0.5 mg. testosterone propionate and in rats receiving 2.5 mg. are essentially the same, indicating that the corpus luteum grows in the same fashion during periods of testosterone injections as it does during the course of pregnancy.

It is observed that the total lipids in the pregnant rat show a slight decrease during the first 16 days followed by a marked rise at the 18th day of pregnancy. About 2 days following littering there is a drop in total lipids which lasts a few days and is followed by a second rise.

The values for cholesterol and ketosteroids, the latter calculated as progesterone, show that the ketosteroid fraction rises only slightly during the first half of pregnancy when progesterone action on the tissue is marked, while it increases sharply during the second half, reaching its highest concentration at about the day of littering. The concentration of cholesterol follows a pattern similar to that of ketosteroid except that it actually decreases during the first half of pregnancy.

Comparison of the results permits the authors' conclusion that the changes in weight and in chemical composition of the corpus luteum in experimentally induced hypertrophy are essentially the same as those occurring in untreated rats during the course of pregnancy.

## VAGINAL RESPONSE TO ADRENAL STIMULATION

JOSEPH SCHILLER (INTRODUCED by F. H. PRATT)

Proc. Soc. Exper. Biol. & Med., 60: 207-10, 1945

In this study, young female rats of the Long-Evans strain were injected daily for 5 days with adrenocorticotrophic hormone (ACTH). Hepatectomy was performed by making an incision parallel to the ribs and extirpating the median and lateral left lobes. Grafting of the adrenals was done by suturing both glands to the spleen. All sections were stained with hematoxylin-eosin and vaginal smears were taken by the lavage method.

The administration of ACTH to normal females gave inconclusive results. Although the estrous phase seemed in some instances to be prolonged, since the diestrous phase was unaffected, it was concluded that ACTH was ineffective in normal female rats.

On the assumption that the liver might inactivate part or all of the estrogenic substances released by the adrenal cortex, further experiments were performed on partially hepatectomized rats. After this procedure, 12 out of 15 animals went into the condition known as "constant subestrus" characterized by the predominance of epithelial cells in the vaginal smear. The injection of ACTH into these responsive ones induced full cornification, indicating that the stimulated adrenals can supplement the estrogenic substances sufficiently to induce full estrus.

In order to eliminate the possibility that the injected ACTH had stimulated the pituitary gland to release gonadotropins, 5 partially hepatectomized rats in constant subestrus were ovariectomized and injected with ACTH for 10 days. The vaginal smear continued to show epithelial and cornified cells throughout the experiment.

Ten non-hepatectomized female rats were subjected to autoplasmic grafting of the adrenals into the spleen. If the liver does inactivate estrogens, then the vaginal smear ought to reflect the same condition as that of adrenalectomized

animals. Contrary to expectations, 9 animals went into "constant estrus," the cornified cells being predominant.

It is concluded that in partially hepatectomized young female rats the administration of ACTH induces the release of small amounts of hormone from the adrenal cortex, affecting the sex organs. 1 figure.

## ARE ANTIHORMONES FORMED DURING PREGNANCY?

J. H. LEATHEM AND A. E. RAKOFF

*Am. J. Obst. & Gynec.*, 51: 97- 99, 1946

Although it would appear that antihormones against pregnancy urine extracts do not develop during pregnancy, the fact that a prolonged amenorrhea occurs in some cases following parturition led the authors to reinvestigate the antihormone problem. The results of their investigations showed that gonadotrophins of homologous source are not antigenic and no evidence is available for an antihormonic cause of amenorrhea following parturition.

The sera from 10 patients, 2 to 4 weeks postpartum, were tested for the presence of antigonadotrophic substances against chorionic gonadotrophin and human pituitary. All tests were uniformly negative.

(Everyone will remember the mild furore and bewilderment excited by the publication of Collip's paper on antihormones some years ago. The validity of this doctrine is still a matter of doubt, and it has been seriously questioned by very competent investigators, such as Zondek and Suls. Moreover, even an apparently antihormonal action has not been demonstrated with some of the hormones with which the gynecologist is chiefly concerned, such as the estrogens and thyroid. It is of interest that Leatham and Rakoff were not able to find any evidence of antihormones against the chorionic gonadotrophins of pregnancy. Certainly we can still feel, on the basis of existing evidence, that the amenorrhea of pregnancy is an endocrine effect and is not an evidence of antihormone production.—Ed.)

## HORMONAL MODIFICATIONS OF SOCIAL BEHAVIOR; THE EFFECT OF SEX- HORMONE ADMINISTRATION ON THE SOCIAL STATUS OF A MALE-CASTRATE CHIMPANZEE

G. CLARK AND H. G. BIRCH

*Psychosom. Med.*, 7: 321-29, 1945

The authors have studied the effects of male and female sex-hormone administration on the dominance status of a male-castrate chimpanzee in a food competition situation. The animal with which the castrate was paired was in intact

male of approximately the same size and age as the treated subject. Methyl testosterone and alpha estradiol were the drugs of choice and the daily dosages during the periods of administration were 50 mg. and 2 mg., respectively, for methyl testosterone and alpha estradiol.

The experiments yielded the following results:

- (1) The dominance status of the castrate was enhanced by male sex-hormone therapy.
- (2) The castrate assumed subordinate status as a result of the administration of female sex-hormone.
- (3) Well established habits of social response were acquired by the animals and these tended to persist after cessation of hormone administration.
- (4) The persistent habits of response could be modified and eventually reversed by appropriate hormone treatment.

At present, information on the mechanism involved in the hormonal modification of behavior is too scant to permit the drawing of final conclusions. However, the deleterious effect of the female sex-hormone on the dominance status of the castrate male chimpanzee seems to warrant the tentative conclusion that the differences which have been found to exist between the chimpanzee and other primate species in relation to the question of sexual status and dominance are the products not of differential hormonal action, but of other factors as yet only sketchily perceived.

(If one may be pardoned a flippant comparison to some of the present day methods of endocrine therapy, this study might suggest that dominance status of a hen-pecked husband could be enhanced by male sex-hormone therapy; that is, if he has been previously castrated.—Ed.)

## THE MENSTRUAL CYCLE

### MENSTRUATION, ITS DISORDERS AND THEIR TREATMENT

JOHN ROCK

New England J. Med., 233: 817-24, 1945

The consideration of menstruation presented in this paper is organized as follows: factors in normal menstruation, character of normal menstruation, disorder in frequency of flow, disorder in duration or amount of flow, disorder in frequency, duration and amount of flow and treatment.

*Factors in Normal Menstruation*—Normal menstruation involves 2 separate endometrial processes. One is the cytologic development of this tissue from a proliferatory to a secretory membrane which then changes to a predecidua. The second process is the establishment of the bleeding potential, the activation of which causes the destruction of the superficial portion of the predecidua.

Proliferation is known to be the effect of estrogen from the growing follicles. Secretion is the result of the addition of gradually increasing amounts of progesterone from the young corpus luteum. The predecidua is the result of the prolonged action of both these hormones and represents the extent to which the imperfect corpus luteum of futile ovulation can transform the uterine lining into the decidua of pregnancy.

The author describes the bleeding potential as the susceptibility of highly differentiated arterioles to products of endometrial catabolism. The combined influence of the estrogen and progesterone establishes the ability to bleed as a normal property of the predecidua. However, progesterone is not essential to the process of flow and this frequently is evolved in the nonsecretory, merely proliferative, endometrium. In man, disappearance of the predecidua without activation of the bleeding potential is not to be expected. Among several thousand patients, the author has seen only one case in which a full secretory endometrium was changed to a subsequently proliferating tissue without an intercurrent bloody flow. Activation of the bleeding potential is dependent on a critical change in the absolute or proportional amounts of the various estrogens. The critical change, in normal menstruation, is made when progesterone which has quickly followed or been active concurrently with an estrogen is withdrawn.

Factors, other than hormonal, that influence bleeding are clotting qualities of blood, nature and rapidity of tissue-repair processes, venous congestion, inflammatory hyperemia, uterine muscle contraction, and, subordinately, elements of diet or hygiene.

*Character of Normal Menstruation*.—Many forms of catamenia must be considered normal, although they differ from the pattern considered to represent perfect menstruation. However, the term "normal menstruation" should be limited to that which follows ovulation. In no woman are the menstrual cycles

male of approximately the same size and age as the treated subject. Methyl testosterone and alpha estradiol were the drugs of choice and the daily dosages during the periods of administration were 50 mg. and 2 mg., respectively, for methyl testosterone and alpha estradiol.

The experiments yielded the following results:

- (1) The dominance status of the castrate was enhanced by male sex-hormone therapy.
- (2) The castrate assumed subordinate status as a result of the administration of female sex-hormone.
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At present, information on the mechanism involved in the hormonal modification of behavior is too scant to permit the drawing of final conclusions. However, the deleterious effect of the female sex-hormone on the dominance status of the castrate male chimpanzee seems to warrant the tentative conclusion that the differences which have been found to exist between the chimpanzee and other primate species in relation to the question of sexual status and dominance are the products not of differential hormonal action, but of other factors as yet only sketchily perceived.

(If one may be pardoned a flippant comparison to some of the present day methods of endocrine therapy, this study might suggest that dominance status of a hen-pecked husband could be enhanced by male sex-hormone therapy; that is, if he has been previously castrated.—Ed.)

*Disorder in Frequency, Duration and Amount of Flow.*—Aperiodomenorrhea, by derivation, means immeasurability and therefore unpredictability of the onset, quality, quantity and duration of flow. This is frequently called "menometrorrhagia".

*Treatment.*—Because there are no efficient methods for controlling ovulation, in cases of oligomenorrhea and in most cases of polymenorrhea, nothing but hygienic measures and encouragement should be used. In polymenorrhea, when the shortening of the cycle is due to a premature decadence of the corpus luteum, daily increments of 0.1 or 0.2 mg. of diethylstilbestrol may be tried. General supportive measures must suffice in hypomenorrhea.

In hypermenorrhea, as in aperiodomenorrhea, endometrial cancer must be ruled out. If hypermenorrhea is of a serious degree, anemia must be relieved, diet be perfected and pelvic congestion be alleviated. If these measures fail, progesterone or testosterone propionate may be tried. Since the condition is usually seen in women over 35, hysterectomy is not seldom the best cure.

The hormonal treatment of amenorrhea and of aperiodomenorrhea is essentially the same. Progesterone is the hormone employed, with the addition of estrogen in cases of amenorrhea.

(Rock has been a leading student of reproductive physiology, and his present review is an excellent one. Especially trenchant, it seems to me, is his statement that, in addition to the purely cytological changes of the cycle, we must remember also that we deal with the far more difficult problem of bleeding potential. The former are fairly well known, being readily revealed by the microscope. The hormonal bleeding potentialities of any particular endometrium, on the other hand, are not to be explained by its histological structure, but by certain hormonal and vascular factors concerning which we still know comparatively little. It seems quite certain that this bleeding potential is a highly individual affair, depending on such intangibles as the activity and the degree of sensitivity or refractoriness of the woman's pituitary and ovaries, a corresponding susceptibility or refractoriness of her endometrium to the ovarian hormones, the behavior of the endometrial blood vessels, the uterine blood vessels, and probably still other factors.

Rock believes, as do most of us, that in women with moderately shortened or lengthened cycles, it is the preovulatory span which characteristically constitutes the variable, while the luteal phase is apparently of fairly constant duration, ordinarily about 2 weeks. Like most writers who know a good deal about menstrual endocrinology, he is obviously unenthusiastic about organic therapy.—Ed.)

## THE ANOVULATORY CYCLE AND MENSTRUATION

ROBERT MEYER

Am. J. Obst. & Gynec., 51: 39-47, 1946

The uterine bleeding, called anovulatory cycle, does not appear at a definite point in the cyclical changes of the follicle and the endometrium. Interruption of the cycle in either causes bleeding both in the early and in the late time of the proliferation stage, and occasionally at any time in the luteal stage.

of constant length however frequently they may approach the rhythm of the lunar month. Most normal cycles are within the range of 28.4 days. However, excursions beyond these limits were found to be not infrequent in a group of 100 normal women. Of 600 cycles observed in these women, 16.5 per cent were beyond the range of 24 to 32 days. In general, the period of menstruation lasts for not more than 7 days and not less than 3, and requires an average of 4 napkins a day. In successive periods of flow the amount and duration of bleeding and the quality of the discharge are variable in the absence of ovulation.

*Disorder in Frequency of Flow.*—One distinguishing characteristic of normality is the periodicity of the recurrent cycles. Except in cases of extreme oligomenorrhea, whenever flow occurs aperiodically, one may be sure that ovulation is incomplete or more infrequent than are the phases of flow. Aperiodomenorrhea is therefore abnormal because it bespeaks a failure of ovulation. As failure of ovulation is dysfunctional, this disorder is dysfunctional. Among the forms of functional, periodic flow are oligomenorrhea, polymenorrhea, hypomenorrhea and hypermenorrhea.

Amenorrhea customarily is absence of menses for 4 months or longer. Amenorrhea is essentially a gross dysfunction of ovulation. When pituitary failure is not evidenced by dysfunction of other endocrine glands, there is usually only partial lethargy of follicles. Although the follicle may approach normal size, the egg does not mature nor is the estrogen decrease sufficient to cause destruction of the endometrium.

Women who menstruate at long intervals, but always similarly, function normally during the 4 weeks preceding onset of flow but before this there is disruption of the reciprocal activity of the pituitary gland and the ovary. This condition is known as oligomenorrhea.

Polymenorrhea is characterized by the periodic occurrence of the flow oftener than every 25th day. Biopsy studies reveal the following significant facts among these patients:

1. Almost all women who flow consecutively as early as the 21st day will be found to have only a proliferative endometrium.
2. Those whose cycles lie between 22 and 24 days show in their endometrium, at the time of flow, a luteal influence of about 14 days' duration.
3. Some women with such short cycles show less than a 14-day luteal influence; the endometrium is secretory but not of the ripe predecidual type.
4. Occasional patients who menstruate every 2 weeks are found to flow alternately from a full secretory and late proliferative endometrium.

*Disorder in Duration and Amount of Flow.*—Hypomenorrhea represents a scanty flow of only one or 2 days' duration. The endometrium is usually not as thick as is commonly found but this condition has not been found to cause infertility.

Hypermenorrhea (prolonged or voluminous phases of flow) may be partially due to nonhormonal factors such as retardation of clotting and tissue-repair. Also, a hormonal disorder may be involved which is thought to be mainly one of luteal secretions.

a gynecologist, who will perhaps then tell the patient that she has been wrong. This is not said in a spirit of flippancy, because certainly mere periodicity in itself is not the sole criterion of genuine menstruation. I mention these things simply to emphasize that there are two sides to the question, and the different hormone mechanisms involved, and the differences in ovarian and endometrial histology are not considered by many to be sufficient to separate them into two separate categories, menstruation and pseudo-menstruation. The term menstruation is of ancient vintage, and until our modern era of endocrinology, has always been a clinical one. The reason for the differences in viewpoint are well expressed in Meyer's statement that "the biologist thinks in terms of etiology and the gynecologist in terms of ultimate ends." Though not a biologist, I have always been inclined to the view that the designation of anovulatory menstruation is not necessarily incorrect. I have often used childbirth as an illustration, and I do not think it far-fetched. The baby is usually delivered by the vertex mechanism, but if the mechanism is very different, as in breech delivery, the process is still childbirth. However, I think I can imagine Dr. Meyer's come-back to this comparison.—Ed.)

## THE RELATION OF THE THECA-CELLS TO DISTURBANCES OF THE MENSTRUAL CYCLE

A. CULNER

J. Obst. & Gynaec. Brit. Emp., 52: 545-58, 1945

Theca-cell proliferation may occur as part of the maturation process in the Graafian follicle.

Theca-cell luteinization around atretic follicles may or may not be without clinical significance in ovulatory cycles, but is nevertheless a part of the normal atretic process. Luteinized theca-cells exert an endocrine influence, the precise nature of which is as yet undetermined. The formation of extensive areas of lutein theca-cells may be visible macroscopically and appear as pale yellow masses or plaques usually associated with atretic or cystic follicles which, however, may not be readily apparent. Luteinization of theca-cells may be localized to small areas and, consequently, serial sections of ovaries may be necessary to determine the presence of luteinized theca-cells.

In the presence of extensive thecal luteinization associated with follicular atresia, disturbances of menstrual rhythm and bleeding may ensue. The term "corpus thecale luteum" has been suggested for the thecal proliferations occurring in association with follicular atresia, and the following classification for the types of these reactions has been proposed:

### I. Corpus thecale luteum.

(a) Without granulosa-cells or with degenerating granulosa-cells. (These give rise to para-lutein or theca-lutein cysts.)

(b) With luteinized granulosa-cells. (These produce lutein cysts usually associated with chorionepithelioma and may be confused with persistent corpora lutea.)

### II. Corpus thecale luteum fibrosum.

The similarities between true menstruation and the anovulatory cycle, namely, the ischemic necrosis and bleeding caused by the nonproduction of hormones, are superficial when compared with the fundamental differences. These latter are stipulated by the revolutionary hormonal, chemicofunctional and morphological preparations of the endometrium for pregnancy. These preparations in the primate differ from those in the lower animals because they must be adapted to different types of placentation. For this reason the regression of the endometrium when fertilization does not occur must necessarily also be fundamentally different, so that one cannot relate estrous bleeding to menstruation.

From the discussion presented in this paper, it seems clear that the results of both the histologic and hormonal investigation of anovulatory bleeding are still grossly incomplete. Although some similarities exist between ovulatory and anovulatory bleeding, the differences are such that a sharp line can be drawn between them. Both might be considered as abortive processes. The anovulatory cycle may be compared to the prepubertal interruption of the developing follicle without bleeding, while the cycle which ends with menstruation is more comparable to the abortion of an early pregnancy. The author points out the close histologic and hormonal relationships between the pregravid stage and the early pregnancy. This is the cardinal point from the gynecologist's point of view, as he will not fail to recognize the significance of the anovulatory cycle.

The fact that experimental biology and gynecology consider the problem from entirely different angles gives rise to their opposing positions. The whole question is not a simple academic argument, but represents the clashing of 2 thought processes. The biologist thinks in terms of etiology while the gynecologist thinks in terms of ultimate ends and will not allow the term menstruation to stand for anything except that which has been traditional. Menstruation is the symbol of sexual maturity and potential fertility. Without corpus luteum there can be no pregravid phase, without which there is no true menstruation. 1 figure.

(Any comment from such an authoritative source as Robert Meyer on the controversial question of the justifiability of the term "anovulatory menstruation" should be welcomed by us all. Meyer and Schroeder have been the chief exponents of the view that the term menstruation should be applied only to cycles associated with ovulation, corpus luteum formation and progestational changes in the endometrium. In other words, only such cycles as fulfill the full physiological purpose of the cycle should be thus included. Most of his paper is devoted to pointing out the differences between the ovulatory and anovulatory types of cycle, and with this discussion everyone will agree. Certainly the hormone mechanisms are different, but the difference of opinion which has arisen has been as to whether the incomplete, unproductive anovulatory cycle should be excluded from consideration as menstruation even when the bleeding is periodic, physiologic in the sense of being produced by the woman's physiological secretions, and when it does not differ in any clinical way from the bleeding of the ovulatory cycle. It is true that anovulatory cycles often, through additional aberration, bring about the pathological functional bleedings, but the same is true, to a lesser degree, of ovulatory cycles.

Every gynecologist who has occasion to perform many endometrial biopsies knows that some women who menstruate with no more irregularity than is true of normally ovulating women are found to have anovulatory cycles. In other words, both patient and doctor would consider these women as "menstruating" unless they happen to fall into the hands of

## VULVA AND VAGINA

### HYDRADENOMA AND HYDRADENOID CARCINOMA OF THE VULVA

GEORGE R. LACY, JR.

Am. J. Obst. & Gynec., 51: 268-71, 1946

The sweat glands of the vulva include, in addition to the common or eccrine glands, a special group called the apocrine glands. The apparent rarity of tumors of the apocrine glands is probably because they have been included in reports with tumors of the common or eccrine glands. Following the classification of Gates, Warren and Warvi, the benign tumor of apocrine gland origin is called hydradenoma papilliferum and the malignant tumor is called hydradenoid carcinoma. In this paper the author presents a case of each type of tumor.

A white woman, 34 years of age, was admitted to the hospital for complaints not referable to a small cystlike structure on the left labium majus midway between the anterior and posterior commissures. The mass was removed. Microscopic examination showed it to be a small tumor mass composed of 2 types of epithelium, one a tall columnar pink cell and the other a cuboidal, dark, blue-staining cell. The entire tumor was surrounded by connective tissue and showed no evidence of invasion. The tumor was located immediately below the surface epithelium. A diagnosis was made of hydradenoma papilliferum of the vulva. Twenty-six months later there had been no recurrence of the tumor.

The second case is that of a 67-year-old white woman who was admitted to the hospital with the complaint of slight vaginal bleeding and purulent discharge for 2 weeks. Examination revealed an ulcerated area overlying the Bartholin gland just within the vaginal introitus on the left. The region underlying the ulcer was indurated but no definite mass could be felt. Microscopic examination of biopsy tissue revealed a mass of small deep-staining cells which grew in solid sheets and showed distinct signs of invasion. Mitotic figures were numerous but the growth was not pleomorphic. A diagnosis of hydradenoid carcinoma of the vulva was made. In spite of simple fulguration with cautery, the tumor has persisted but there are no evidences of regional or distant metastases.

According to Novak, 40 cases of hydradenoma of the vulva had been reported before 1940 and since then an approximately equal number have been reported. Grossly the tumors are usually under one cm. in diameter and are nearly always single. They may be of the solid adenomatous type but more often are papillary in nature.

Hydradenoid carcinomas are of low malignancy and diagnosis of the case described above is made chiefly by exclusion. Extension from the cervix, Paget's disease and hair matrix carcinoma must be considered in the differential diagnosis. 4 figures.

III. Corpus thecale luteum candicans.

IV. Corpus thecale luteum hyalinum.

V. Corpus thecale luteum restiforme.

In Group I the original form of the follicle is retained, the granulosa-cells may be degenerating; the theca may, in part, retain stromal features and hyaline deposition may have occurred between the theca and basement layer of granulosa cells or their remains. In Group II granulosa cells are not present, absorption of liquor folliculi has taken place, the cavity is filled with a few connective tissue cells and a hyaline ring may be found around these cells. External to the ring are the luteinized theca-cells. Group III represents lutein reactions occurring around a collapsed corpus atreticum in which the hyaline laminae of opposite sides, when they exist, become opposed with obliteration of the central cavity. In Group IV there is a lutein reaction surrounding follicles in which collapse has not occurred, but hyaline tissue invades the cavity with a few nucleated connective tissue cells. Group V indicates a lutein reaction around primordial or small maturing follicles. These were not observed but are theoretically possible.

The character of the uterine reactions associated with theca-cells is such that neither estrogenic nor progestogenic influences can be attributed to them. Their activity suggests the formation of a 3rd ovarian hormone which may exert androgenic activity, or of a modified secretion of the known varieties which is capable of distorting the balance between simultaneously acting steroid hormones of the menstrual cycle.

The virilizing effect of certain lipid-cell tumors of the ovary, theca-cell tumors and lutein thecomas is not without its counterpart in the follicular theca-cell proliferations. These latter are prominent at the menarche and menopause. It is also apparent that the histological features of the cellular components of some theca-cell tumors are in no way radically different from the exaggerated theca-cell proliferations observed in follicle atresia. 11 figures.

(While it may be true that luteinized theca-cells exert an endocrine influence, I know of no evidence on this point, certainly as applied to the usually moderate degrees of luteinization so often seen in atretic follicles. It is with these that Culiner's paper is chiefly concerned. Every gynecological pathologist must have wondered as to their significance and why, in one and the same ovary, some atretic follicles show such changes and others not. My own thought has been that only at certain phases of follicular development or degeneration are the theca-cells sensitized to this luteinizing influence.

The rather elaborate classification suggested by the author does not commend itself, and I believe that most of the "types" enumerated represent different phases of the same process. As for the multiple lutein cysts seen with hydatidiform mole or chorion-epithelioma, these may be of either granulosa or theca lutein type, or a combination of the two. In the most marked case I have ever seen, all the cyst locules showed only theca lutein cells in their walls.—Ed.)

posed of different types of tissue, some of which are heterologous. Thus, besides the spindle cells with varying amount of blood or lymphatic vessels and the myxomatous changes, there are fibrillar connective tissue, cartilage and occasionally muscular tissue of both types, mainly the striped variety. According to Ewing, in some cases the rhabdomyoma constitutes almost the only element seen in the polypoid sarcoma of the vagina of infants. As a matter of fact, Kolisko found muscular tissue in his 3 cases and believes it never to be absent.

These tumors are commonly spoken of as sarcomas botryoides, owing to the polypoid form, with large base of implantation. They have a typical grapelike aspect.

Of the various theories proposed to explain their genesis, the authors are inclined to believe that that of Wilms offers the most satisfactory explanation. Wilms considers these neoplasms as mixed tumors of fetal origin; derived from an embryonic germ in a stage of undifferentiation, consisting of mesodermal and mesenchymatous cells originating from the renal region and isolated in the vaginal wall. In fact, the frequency with which these tumors occur in infants, their extremely varied histologic aspect and the embryonic character of their tissues suggest that they derive from residual embryonic cells.

These tumors usually localize on the anterior vaginal wall, and as they grow they fill the whole vaginal canal, spread anteriorly and superiorly, invade the bladder, periuterine cellular tissue and, less frequently, the lymphatics. Metastases in distant organs are exceptional.

As a matter of diagnosis, the possibility of sarcoma ought to be born in mind whenever an infant presents bloody discharge from the genitals, especially when there is a polyp protruding through the hymen. Thorough microscopic examination should be made, preferably of many sections.

The prognosis is very grave, as the disease is practically always fatal. Only 2 cases have been reported in the literature as being cured: Volkman's case following radical operation and that of Döderlein and Warner, after removal of the greatest portion of the tumor and radium treatment.

Concerning treatment, a wide resection including the largest possible amount of normal tissue should be done, followed by radium therapy. The authors believe electro-surgery to have a valuable application in these cases.

(While this tumor type is very rare, it is of great interest, especially from the standpoint of histogenesis. The theory of Wilms, mentioned by the authors, seems to be the most plausible one. According to this, the tumors arise from undifferentiated mesonephric mesodermal elements pulled down into the Müllerian area. I have had the opportunity of studying tissue from 4 of these cases, including one from South America which was sent to me through the kindness of Dr. José Medina, the professor of gynecology and obstetrics at São Paulo, Brazil. In one of these patients whom I later saw clinically, previous excision and radium therapy had been done, but the growth continued in spite of these. When I saw the patient, a foul gangrenous mass protruded through the vagina, so that parts of it could literally be plucked off with the fingers. She died shortly afterward. While all authors speak of the frequency of striated muscle in these tumors, it is sometimes lacking, and when present is most commonly of embryonic type, so that it can readily be missed on microscopic examination.—Ed.)

(The correct name of this vulvar tumor is hidradenoma and not hydradenoma. It is rare, but it is a rather important lesion because its histological appearance bears a strong resemblance to adenocarcinoma, for which it has often been mistaken. However, it is a benign lesion and there is only one case in the literature, that of Eichenberg, in which there was good evidence of clinical malignancy. Recent reports have increased the number of cases in the literature to approximately 80, but it is quite certain that many cases are unreported or unrecognized. It is unfortunate that in a recent report of a large group of obviously benign hidradenomas the designation of adenocarcinoma was applied. The April issue of the Survey contains an abstract of a rather complete study of this lesion with a report of 15 new cases, by Novak and Stevenson (p. 251).—Ed.)

## SARCOMA OF THE VAGINA IN A GIRL EIGHTEEN MONTHS OLD

ISIDRO BOLLA, DOMINGO MOSTO AND ERNESTO V. MARISCO

An. d. Inst. matern. y asist. social, Buenos Aires, 6: 40-49, 1944

The authors report the case of an 18 months old girl first seen on September 16, 1940, complaining of genital bleeding following a trauma. On examination, a small purple tumor showing the so called contact bleeding could be seen through the hymen in the vagina. A biopsy showed it to be a "fibroleiomyxosarcoma of the vagina".

Twenty days later the patient began to have trouble in urinating and the tumor had grown more in size, causing discharge and staining. It was spherical, the size of a walnut, having a thick pedicle attached to the anterior vaginal wall with infiltration at this level extending upwards and laterally. The cervix seemed to be normal. An x-ray picture of the thorax was negative. With the aid of an electric scalpel, the tumor was removed together with the portion of vagina circumscribing its pedicle.

Convalescence was uneventful, but on December 6, 1940, the patient presented increasing symptoms of urinary retention and had been losing weight. Radium treatment, advised after operation, had not been carried out. Examination revealed recurrence of the tumor at the same place with extension to the neighboring tissues. The child died in April, 1941, 7 months after the operation, with urinary infection.

Vaginal sarcomas occurring in children are rarely seen. Some of their peculiar aspects, such as their frequency, very rapid evolution, histopathologic characteristics and prognosis, tend to distinguish them sharply from the sarcomas occurring in adult vaginas. There are already more than 70 cases reported in the literature. They are more commonly seen between the ages of 18 and 30 months, although they may occur earlier in life or much later, close to puberty.

Histologically they can be divided into 2 large groups: (1) Simple tumors, consisting of only one type of tissue, usually showing spindle-shaped cells with myxomatous degeneration; and (2) Mixed tumors, by far the more common, com-

specific therapy has not yet been completely solved by the use of any one agent or drug.

According to Zahorsky, in true gonorrhea the child is acutely ill for a few days and often has fever; the genital tract becomes intensely inflamed and swollen, and a thick creamy pus is discharged from the vagina. This writer finds the incidence of true gonorrhea in his practice to be less than 10 per cent of all cases, as affirmed by positive cultures. Another writer finds an incidence of only 22 per cent positive by culture in 1715 child patients suffering from a vaginal discharge. However, Beckman finds the incidence of gonorrhea in female children to be high, running perhaps second to measles.

Although most authorities admit culture to be far superior to smears for diagnosis of infection and cure, a majority insist on absence of discharge or discharge free from pus cells, 3 negative weekly smears and negative smears and cultures at 3 to 4 weekly intervals for at least 4 months after evident clinical cure. Complications affecting cure are urethritis and proctitis. Also, the cervix may be a site of infection and deep infected vaginal rugae may act as a reservoir.

Almost complete confusion is manifested in attempts to evaluate the great variety of treatments. Chemical agents have rather fallen into disrepute, antiseptic douches or instillations being considered to retard rather than accomplish cures. Estrogen therapy has received considerable attention in the literature. After 2 weeks of estrogen administration to establish the adult type of vaginal mucosa, about 4 weeks are required to return to normal so that the effect on the gonococcus and the recurrences may be held in a latent state until retrogression is established. Apparent cures are estimated at 80 to 100 per cent while recurrences vary from 25 to 70 per cent.

The sulfonamides and penicillin have received wide attention with reported success. However, more time is required to establish the therapeutic value of both in cases of gonorrheal vaginitis in children.

(The author does well to call attention to the still existing differences in viewpoint and in practice concerning the problem of gonorrheal vulvovaginitis, in spite of the genuine advance made in recent years. There are still many who employ estrogen therapy, which undoubtedly yields a very high percentage of cures. But there appears to be a growing tendency to supplant this with sulfa and penicillin therapy, and the father of the estrogen plan, Robert Lewis, has himself made such a switch. We are not yet quite ready for a final evaluation on this point, and there would seem to be no objection to the double-harrelled combination of the two plans.—Ed.)

## CONSIDERATIONS CONCERNING SULFANILAMIDE TREATMENT OF VAGINAL TRICHOMONIASIS

ABRAHAM ALEXENICER

An. d. Inst. matern. y asist. social, Buenos Aires, 6: 190-94, 1944

Impressed with the good results reported at the University of Brazil, Rio de Janeiro, with the use of sulfanilamides in the therapy of vaginal trichomoniasis,

# SULFANILAMIDE AND SULFATHIAZOLE ABSORPTION VIA RECTUM AND VAGINA; FURTHER STUDIES

GEORGE L. CARRINGTON

Am. J. Obst. & Gynec., 51: 90-96, 1946

In the present study, the author concludes that sulfanilamide and sulfathiazole, separately or together, are absorbed variably from the rectum and vagina.

When compared with previous studies, present results show a definitely higher and more constant level of the drug in the blood after intraperitoneal use than after rectal or vaginal administration. Within the limits of the previously recognized variations of absorption, the blood levels of sulfanilamide vary directly with the amount of the dry powder placed in the rectum. However, in vaginal administration, when the amount of dry drug was increased, the blood levels were less during the first 2 days after operation, later rising to levels comparable to when less drug was used. Apparently moisture was the factor concerned.

It was found that sulfathiazole is absorbed in a similar manner from vagina and rectum. Mixing of the 2 drugs appears to have little effect upon their absorption, though the blood level after rectal administration was somewhat less than for either of the drugs when given singly.

The absorption is hastened when the drug is inserted as a moist paste. A mixture of the 2 drugs should be moistened beyond the "plaster" stage when used in the vagina.

It is suggested that local gonorrheal infections in women might be treated advantageously with sulfonamides via the vagina. 1 figure.

(While it is no doubt true that sulfanilamide and sulfathiazole are absorbed from the vagina, as they are from the peritoneum, it has apparently been established that the beneficial effects are not exerted locally, but through the increased blood concentration which is brought about. Since these general effects can be brought about very effectively by oral administration, there would seem to be no advantage in such local administration in the vagina as has been suggested by the authors. The same principle applies to the peritoneal use of the sulfa drugs, which in itself is rather messy and may increase vascularity of tissues. Formerly a good many gynecologists, including myself, introduced sulfanilamide beneath the peritoneal flap and in the cul-de-sac as a part of the technique of panhysterectomy, but this practice, for the reasons mentioned above, has long been discontinued.—Ed.)

## GONORRHEAL VAGINITIS IN CHILDREN

CHARLES F. NAEGELE

Arch. Pediat., 62: 516-22, 1945

The author attempts to show in this paper that the subject of gonorrheal vaginitis in children is by no means a closed issue. The relative incidence of the condition is disputed; methods of establishing a positive diagnosis for the infection and for a permanent cure have not been standardized; and the problem of

specific therapy has not yet been completely solved by the use of any one agent or drug.

According to Zahorsky, in true gonorrhea the child is acutely ill for a few days and often has fever; the genital tract becomes intensely inflamed and swollen, and a thick creamy pus is discharged from the vagina. This writer finds the incidence of true gonorrhea in his practice to be less than 10 per cent of all cases, as affirmed by positive cultures. Another writer finds an incidence of only 22 per cent positive by culture in 1715 child patients suffering from a vaginal discharge. However, Beckman finds the incidence of gonorrhea in female children to be high, running perhaps second to measles.

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ABRAHAM ALEXENICER

An. d. Inst. matern. y asist. social, Buenos Aires, 6: 190-94, 1944

Impressed with the good results reported at the University of Brazil, Rio de Janeiro, with the use of sulfanilamides in the therapy of vaginal trichomoniasis,

the author decided to try its effectiveness in this common type of infection, and reports in this paper the results he obtained in 26 cases.

Treatment was carried out as follows: thorough cleansing of the vagina with sterilized gauze in order to remove all secretions, followed by the insertion of 2 vaginal suppositories of sulfanilamide, one in each fornix, and the introduction of a gauze tampon. The latter is removed the next morning, followed by the use of a plain water douche (one liter of boiled water). The treatment is continued daily for the next 5 or 6 days. A smear is then made, which will usually prove to be negative. The microscopic examination ought to be repeated several more times in order to assure the cure.

All 26 patients were cured following this plan of treatment, despite some of them having only received 2 or 3 applications. Leukorrhea and pruritis are greatly improved within the first day of therapy.

(It is probably too early to decide whether local sulfanilamide therapy in vaginal trichomoniasis will be a worthwhile addition to the many methods already employed for this pesky gynecological condition, especially in view of the increasing opinion that the good results of sulfa therapy in general are not due to any local effect upon the organisms but to the systemic effect dependent on blood concentration. A somewhat similar plan, employing an ointment of sulfanilamide, allantoin and lactose, was recently described by Angelucci (Angelucci, Helen. *Am. J. Obst. & Gynec.*, 50: 336, 1945, abstracted in the February issue of the Survey, p. 103).—Ed.)

## THE UTERUS

### MALFORMATIONS OF THE UTERUS; REVIEW OF THE SUBJECT, INCLUDING EMBRYOLOGY, COMPARATIVE ANATOMY, DIAGNOSIS AND REPORT OF CASES

JULIUS JARCHO

Am. J. Surg., 71: 106-66, 1946

Since malformations of the uterus are referable to developmental arrest or deviation of the Müllerian ducts, the author presents a brief review of the embryology of these structures.

It has been suggested by Curtis, Rogers and Blocksom that both defective germ plasm and unfavorable embryonic environment are among the most important causative factors. The author believes that various types of uterine anomalies can be attributed to abnormal fusion or lack of fusion, in whole or in part, of the Müllerian ducts. In regard to the time of occurrence of uterine anomalies, Schattenberg and Ziskind remark that the only malformation that occurs after the 5th month is uterus arcuatus.

The author proposes the use of the following classification of the types of uterine malformation: (1) Uterus didelphys; (2) uterus duplex bicornis bicollis, vagina simplex; (3) uterus bicornis unicollis, vagina simplex; (4) uterus septus; (5) uterus subseptus; (6) uterus arcuatus or cordiformis; and (7) uterus unicornis.

*Uterus Didelphys.* This anomaly, in which there is duplication of the vagina cervix and uterus, is comparatively rare. Its clinical importance is its relation to pregnancy and labor. While fertility and pregnancy are not markedly affected, the chances of normal birth at term are greatly reduced. Findley found that abortion is relatively common in cases of uterus didelphys and that labor is prolonged as a result of poor muscular development in the uterus, a small rigid cervix and the encroachment of the non-gravid uterus. Though quite rare, twin pregnancies have occurred in women with uterus didelphys. Corbet records a case in which each uterine component behaved as an independent unit and went into labor at a different time.

*Uterus Duplex Bicornis Bicollis.* This type of abnormality differs from uterus didelphys chiefly in the fact that duplication of the vagina is absent. In general, it may be said that conditions applying to uterus didelphys are applicable to this anomaly as well.

*Uterus Bicornis Unicollis.* In this abnormality, fusion is complete to a point above the cervix, the uterus being widely bicornate. Pregnancy may occur in either or both horns. As a rule, the non-gravid horn produces a decidual membrane which often is expelled without disturbance of the gravid horn. The chief complications in pregnancy are hemorrhage and incarceration of one of the horns during labor. Special complications may arise when one of the horns is rudi-

mentary. It has been indicated that 80 per cent of rudimentary horns possess a canal which does not communicate with the vagina. A rudimentary horn may act much like a tubal pregnancy with all the inherent dangers.

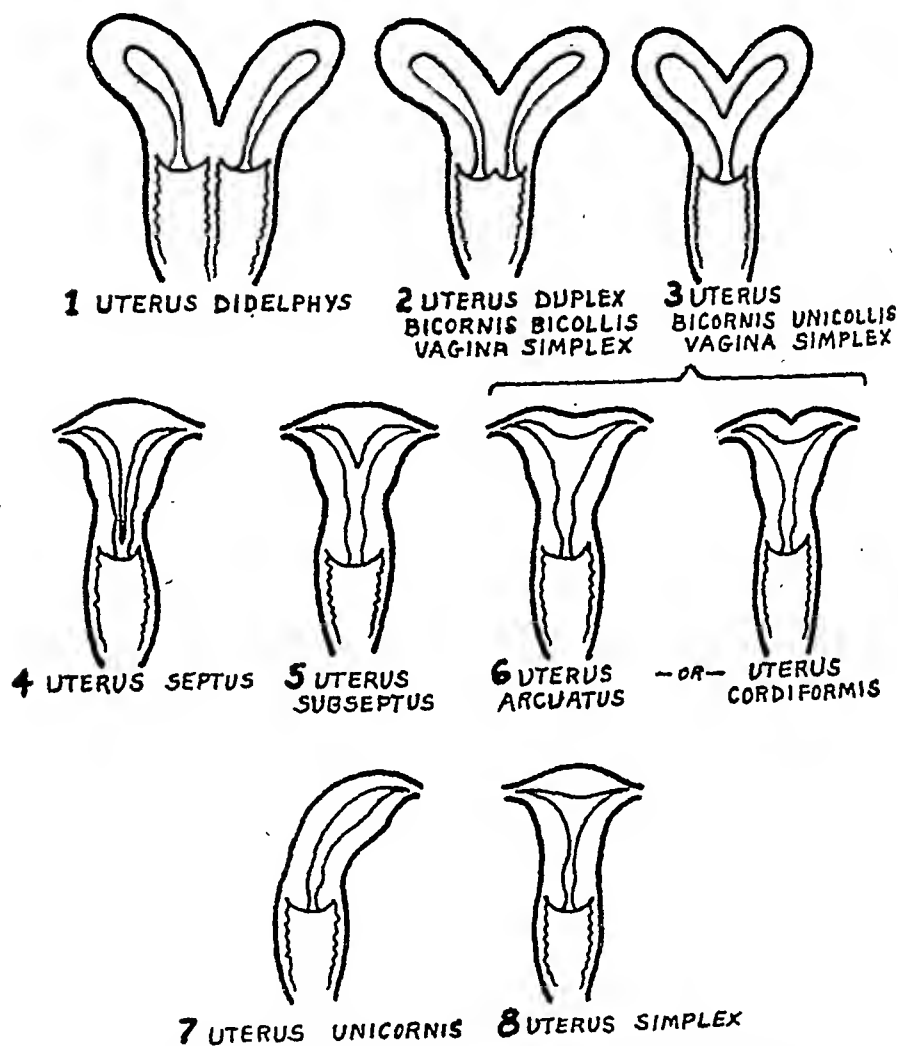


FIG. 2. Normal uterus and seven types of malformation of the uterus and vagina

*Uterus Septus.* In this condition, the outward appearance of the uterus is normal or may present a mild depression in the fundus. Internally there is a septum which divides the cavity, usually extending for the length of the uterus. The danger of uterus septus lies in the fact that if pregnancy takes place in one half, the uterine wall of the other half hypertrophies and by its mere bulk may obstruct delivery from the pregnant half.

*Uterus Subseptus.* As a rule, this does not cause dystocia but occasionally may produce transverse or oblique presentation of the fetus.

*Uterus Arcuatus (Cordiformis).* Externally, uterus arcuatus is marked by a fundal concavity. Where the line of demarcation is deeper and more definite, giving rise to a heart-shaped fundus, the malformation is generally referred to as uterus cordiformis. Uterus arcuatus is one of the most common of uterine anomalies with a high incidence of clinical abnormalities. The complications of pregnancy include prematurity and postmaturity while the complications of labor are prolonged first stage, breech and transverse presentation, sudden intrauterine fetal death and retained placenta.

*Uterus Unicornis.* This abnormality, caused by unilateral suppression of the Müllerian duct, is very uncommon and pregnancy in these cases tends to be uneventful.

The comparative anatomy of uterine anomalies is discussed and the parallel is drawn between these malformations in the human female and the existence of similar forms in lower animals.

Considering the fact that many cases of uterine malformation are observed only at autopsy or accidentally during operation, and that other cases are discovered only in the event of an abnormal occurrence during pregnancy and labor, it is evident that a large number of cases must remain unsuspected and undiscovered. Moore believes that the incidence of such anomalies is much higher than the records would indicate. He concludes, from private records, that one in 500 or 600 women present some definite congenital deviation from normal in the generative tract.

The symptoms associated with genital anomalies are discussed. Prior to pregnancy, menstrual disorders are frequently encountered in double uterus. Dysmenorrhea is an important diagnostic aid in cases of bifid uterus. During pregnancy, in cases of bicornate uterus, the non-gravid horn usually forms a decidua. Sometimes the non-gravid horn continues to menstruate. The proportion of twins is greater in women with double uterus than in normal women. Kelly stated that 11 per cent of cases of sterility are attributable to developmental anomalies of the generative organs.

Patients with uterine malformations show an increased tendency to abortion. The treatment for pregnancy in a rudimentary horn, once diagnosed, is immediate laparotomy and prompt removal of the gravid uterus. In cases of uterus didelphys, it has been reported that 40 per cent have complicated deliveries at term. The complicating factors are listed as: enlarged non-gravid uterus; vaginal septum; uterine inertia; tetanically contracted uterus; retention complications; and eclampsia. In the management of pregnancy complicated by double uterus, it should be remembered that the relatively thin uterine wall presents a constant threat of rupture if labor is long or difficult.

The indications for cesarean section occur more often in patients with uterine malformations.

Methods of diagnosing uterine anomalies are discussed with emphasis upon the advantages of uterosalpingography. The author has introduced a special instru-

ment for uterosalpingography, the pressometer. This instrument facilitates the introduction of gases and opaque media into the uterine cavity and measures the amount of pressure under which the opaque medium is introduced as well as the quantity injected.

Surgical operations in cases of uterine malformation vary widely and no fixed rule or type of operation is applicable since the extent of malformation varies in individual patients. Wherever possible, surgical intervention should be conservative.

The author presents a series of case histories. 38 figures.

(This is an excellent review of an important subject, presenting it in a systematic fashion, even though new important facts are included. The author is well known for his pioneer interest in uterosalpingography and it is perhaps natural that he advocates its employment even in the not infrequent cases in which the diagnosis of genital anomalies is made readily enough without resort to this method.—Ed.)

## DOUBLE UTERUS AND DOUBLE VAGINA; IDENTICAL DOUBLES DEMONSTRATED BY COLPOHYSTEROSALPINGOGRAPHY

R. R. KILLINGER AND H. B. McEVEN

Am. J. Obst. & Gynec., 51: 121-24, 1946

Simple and uniform nomenclature for describing abnormalities of the female genital tract is advocated and the following classification is presented:

1. Uterus arcuatus.
2. Double uterus with a single cervix.
3. Septate uterus with a single or a septate vagina.
4. Double uterus with a double cervix.
5. Uterus with rudimentary horn or absence of one horn.

Taylor estimated that the deformity occurs once in about 1500 obstetric cases and once in about 2000 gynecologic cases. It is suggested that these anomalies occur more frequently than is generally believed. Helpful diagnostic signs in this condition are "irregular menses, dyspareunia, repeated unexplained abortions or miscarriage, and repeated malposition of fetus." Uterosalingograms yield the most complete information available. The authors advise the routine use of roentgen pelvimetry as a diagnostic aid.

A case is presented of a 24-year-old woman who complained of nervousness, pain in the lower part of the abdomen aggravated by intercourse, irregular menses, severe menstrual cramps and sterility. On examination of the genital tract it was noted that a complete septum was present in the vagina extending down to within  $\frac{1}{2}$  inch of the external orifice. Two distinct cervixes were palpated. During the first menstrual period, the flow was demonstrated coming equally from the separate cervixes. The roentgenologic report was most conclusive. Following injection of iodochlorol into the cervixes through a catheter,

2 cervixes, 2 cervical canals, 2 separate uteri and 2 tubes were clearly outlined in the roentgenogram. There was only one tube to each of the separate uteri. Roentgen study of the urinary tract showed no evidence of reduplication of kidneys or ureters. Roentgen examination of the chest and roentgen pelvimetry were normal. 1 figure.

(Innumerable variations of genital duplication, usually of the incomplete variety, may be encountered by either the gynecologist or the obstetrician, although they are relatively uncommon. Even the minor uterine anomalies, such as the uterus arcuatus, may be of obstetrical importance, as Falls particularly has urged. While the more marked grades, such as uterus bicornis or uterus didelphys, are not incompatible with normal pregnancy and labor, they may, on the other hand, result in repeated miscarriage or in serious blockage of the birth canal.

The simplest of this group of anomalies is duplication of the vagina, which may occur in the entire absence of any uterine abnormality. In such cases the septum may be placed to one side of the cervix, so that one vaginal canal leads into the cervix, while the other ends blindly. A good many years ago I saw such a case because of the patient's sterility. This was readily explained by the fact that, just by chance, the husband had used the blind canal, and pregnancy followed soon after excision of the septum. I suppose if I had been smart I would have retained both canals, simply instructing the couple as to which to use when pregnancy was desired and which to employ when pregnancy was to be avoided. I throw out this idea gratis to anyone who wishes to create such a double purpose vagina through the simple construction of a median septum.—Ed.)

## A REVIEW OF THE PROBLEM OF CANCER OF THE CERVIX SINCE THE USE OF RADIUM IN 1912

BROOKE M. ANSPACH

*Am. J. Obst. & Gynec.*, 50: 681-90, 1945

The early treatment of cancer of the cervix was attempted mainly by radical operation. The adoption of radium in 1912 as a treatment of choice by Kelly and Burnham marked the beginning of an epoch. The gamma rays from a radium salt or a radium emanation and the gamma rays from the x-ray have been important therapeutic factors ever since and, to a very considerable extent, have taken the place of radical surgery.

The extent of the lesion at the start of observation and treatment is of much importance. Cancer statistics have shown that the earlier the lesion is found the more effectual were all forms of treatment. It may be concluded that a greater number of cancer patients are presenting themselves for treatment in the early stage as a result of information given to the lay woman and to physicians in general. The proportion is almost bound to increase.

Biopsy of the cervix or diagnostic curettage with histological examination remains the trustworthy diagnostic criterion. The color test of Schiller, the colposcope of Hinselman, and the vaginal smear method of Papanicolaou and Traut, the last the most effective of the 3, direct attention to suspected patients.

Screening of the radiant substances is of the greatest importance since the irradiation must be effected just where it is needed with ample protection of the surrounding areas. A sufficient supply of the radium salt or its emanation must be on hand at the moment of application. The dose for cervical cancer is 3600 mg. hr. and upwards with 1.5 mm. of platinum screening. A "massive dose" at the first treatment has been the trend for a long while; nevertheless, some authorities have reported excellent results with smaller and repeated applications. Deep x-ray therapy has acquired a position as a desirable preliminary or adjunct to nearly every application of radium. Theoretically, it should be first. The histologic diagnosis must be settled before any form of irradiation is started. Among the radiologists, the work of Heyman is presumed not to have been surpassed. It is concluded that irradiation with radium or its emanations, or by deep x-ray, will become more widely and adequately available, better understood, and more effectual.

The advance radical hysterectomy for cancer of the cervix is a formidable operation. Since the appearance of irradiation the necessity for radical operation has been changed. Bonney has succeeded Wertheim as the outstanding exponent of radical surgery. It is interesting to note that Wertheim in 1911 had an absolute 5-year salvage in 250 patients of 18.1 per cent, and that Bonney in 1941 reported his absolute 5-year salvage in 500 operations as 25 or 26 per cent. The risk attending operative procedure has been much reduced and improvement is likely to continue. Of the 93 patients lost by Wertheim in his first 500 operations, the cause of death in 39 was put down as peritonitis. With the sulfonamides, penicillin and streptomycin, with the use of glucose, plasma and transfusion, with Wangenstein's drainage, continuous spinal anesthesia and prostigmine—a large proportion would have been prevented.

Whether a combination of surgery and irradiation as practiced by Lynch and Taussig will accomplish more than radium or surgery is a question for the future. Perhaps a combination of irradiation with operation may be devised that will be more effective than either alone.

(The author of this paper is well qualified by his long experience in this field to review and appraise the problem of cervical carcinoma. His experience goes well back to the early days of radical operation, for he was long associated with John G. Clark, one of the pioneers in this field. Anspach himself has contributed many valuable studies, especially in the field of radium therapy. The present paper is an authoritative evaluation of the cancer problem as it stands today.—Ed.)

CARCINOMA SUBSEQUENT TO THE RADIOTHERAPEUTIC  
MENOPAUSE

J. A. CORSCADEN, J. W. FERTIG AND S. B. GUSBERG

Am. J. Obst. &amp; Gynec., 51: 1-12, 1946

Among 958 patients who had been treated for benign uterine bleeding by the radiotherapeutic menopause and followed for an average of 6.7 years each, there subsequently occurred 15 carcinomas of the uterus. Based on modified mortality statistics, the same number of women in the general population during the same length of time should contract 4.4 carcinomas of the uterus. The number of cases observed is therefore 3.4 times as great as the number expected.

Two and eight-tenths per cent of women in the general population between the ages of 30 and 55 years contract cancer of the uterus before reaching the age of 80. Applying the above ratio of 3.4, one finds that 9.6 per cent of women suffering from uterine bleeding prior to the menopause would contract the disease.

Of the 15 cases of uterine carcinoma, 9 were of the corpus and 6 were of the cervix. This abnormal preponderance of carcinoma of the corpus is in agreement with that present in other reported cases in which the ratio is 2 of the corpus to one of the cervix. This ratio of corpus to cervix is 6 times that obtaining in the authors' clinic.

The question may be raised as to whether these cancers were truly "subsequent" to the original procedure or whether they were present at the original treatment and overlooked. Since the 6 cases of cervical cancer here reported occurred 6 years or more after the original treatment, all of them would be classified as "subsequent". However, cancer of the corpus may lie quiescent for a longer time and the determination of whether or not it was coincident with the original treatment is more difficult. In the cases here reported the intervals were 2, 4, 9, 9, 9, 10, 10, 13 and 21 years, respectively. In the patient with the 2-year interval, the authors believe, from personal handling of the case and curettage, that the adenocarcinoma was not present at the original treatment.

Inhibition of cancer by intrauterine radium and by the application of x-ray seems unlikely in these cases with the possible exception of one case in which intrauterine radium was employed with carcinoma appearing 4 years after the original treatment. To the question as to whether the radiation employed might be a contributing cause of the carcinoma, the authors refer only to extensive evidence in the literature which indicates that radiation with techniques and dosages such as were employed in these cases is not a cause of carcinoma.

It is inferred that the endometria of uteri which bleed abnormally prior to the menopause are predisposed to the subsequent development of carcinoma of the corpus. Prophylaxis against carcinoma of the uterus should be an important factor in a plan of treatment for uterine bleeding prior to the menopause.

(This impresses me as a very valuable study. The authors not only report a sizable group of cases in which women who had previously had a radiotherapeutic menopause in-

duced for benign bleeding developed cancer in later life, but also show that the chances for such a sequence are 3.4 times that of the normal cancer incidence. These figures are made more impressive by the fact that it is especially adenocarcinoma of the corpus, rather than carcinoma of the cervix, which is the more likely to develop in such a group. These findings may not be unrelated to those of others who, like Crossen and Hobbs, (*J. Missouri M. A.* 32: 61, 1935) find that women who have had late menopause show a greater later tendency to adenocarcinoma of the body than those in whom the menopause had occurred at the usual age. Certainly there seems to be justification for the authors' viewpoint that prophylaxis, with perhaps special emphasis upon educational measures, is especially important in women who give a history of functional menopausal bleeding.—Ed.)

## CARCINOMA OF THE CERVIX; AN ATTEMPTED FOLLOW-UP STUDY OF 500 CASES. II. THE RESPONSIBILITY OF THE MEDICAL PROFESSION FOR THE END-RESULTS

PETER GRAFFAGNINO AND ELIZABETH M. McFETRIDGE

New Orleans M. & S. J., 98: 351-59, 1946

The present paper is the second in a series of 3 papers on an attempted follow-up study of 500 patients with carcinoma of the cervix treated at the New Orleans Charity Hospital over an approximately  $5\frac{1}{2}$  year period ending July 1, 1937. Important data concerning these 500 patients may be summarized as follows: One hundred and eighty-three of the 500 women were white and 317 were negro. The age range was from 20 to 78 years. Approximately two-thirds of the patients were between 35 and 55 years of age at the onset of symptoms but 18 per cent were under 35 years of age. Forty-three patients had no treatment at all. Ideal treatment, according to modern criteria, was carried out in only 28 patients, and even by considerably lower arbitrary criteria only 194 patients had treatment that could be considered in any way adequate. Eleven patients were treated surgically, only one of whom was submitted to the Wertheim operation.

Of the 397 patients on whom a follow-up could be secured, 358 are known to have died, 2 of whom survived for 5 and 7 years, respectively, without recurrence and died of non-cancer-connected causes, and 39 are known to be alive for periods varying from 7 to 12 years after treatment. Included in the entire series are 29 cases of carcinoma of the cervical stump; 4 of this group are among the survivors.

In evaluating these sorry results, the fact must be borne in mind that during the period covered by this study, the amount of radium and the facilities for high-voltage therapy were totally inadequate for the patient load. The authors offer certain criticisms and comments concerning the use of the available facilities during the period covered by this study. First, when carcinoma of the cervix is associated with pelvic infection radium is contraindicated and the whole reliance must be upon deep-voltage therapy. This risk seems to have been overlooked in a number of cases in this series; 4 patients died of peritonitis following radium application and in at least 3 of these, the presence of pelvic infection should have been suspected from the history. Also, at that time, decisions as to the amount

of radium required in each case and as to whether or not it should be preceded or followed by deep-voltage therapy were not controlled or standardized. Many of the patients did not receive irradiation over concentrated periods of time. The rationale of surgery in 10 of the 11 cases in which surgery was done is not clear. Two of the 10 were treated by vaginal hysterectomy, 7 by complete hysterectomy and one by supravaginal hysterectomy with conization of the cervix. However, regardless of the available facilities during the period covered by this study and regardless of how they were used, most of the patients died for other and far more basic reasons than improper therapy.

The chief reason why these patients died is because of the stage of their disease when they applied at the hospital for treatment. The authors list the circumstances in 27 cases in this connection, showing the diagnostic errors which were made by physicians outside the hospital. Instances are also cited of diagnostic errors within the hospital. The authors believed that the basic fault in these cases is obviously the concentration of specialists on their own fields, to the exclusion of other fields. Certain patients were admitted to other services after treatment on the gynecological service and, the pelvic state being completely overlooked, were treated for non-pelvic conditions.

The atypical character of certain cases often resulted in lack of suspicion. It must be remembered that carcinoma of the cervix can occur in patients under 30 years of age. Although discharge and spotting are usually the first symptoms of carcinoma of the cervix, the following first symptoms were noted in certain patients in this series: pain, loss of weight, chills and fever, serious hemorrhage, rectal and urinary symptoms, intestinal obstruction, and a blow or fall which called attention to the existing symptoms.

In regard to histologic diagnosis, if the clinical evidence does not agree with the histologic report, the clinical evidence should be accepted as probably correct and the investigation should be continued until a definite diagnosis can be reached.

The question is raised as to whether the attitude of the medical profession toward carcinoma of the cervix is correct. In many instances in this series it suggested deep pessimism, while in others it suggested a lack of realization of the urgency of the disease.

The validity of cancer statistics, in the light of certain facts revealed by this series, is questioned. Some of the death certificates were filled out by physicians who had no knowledge of the past history and apparently did not investigate it.

The 29 cases of carcinoma of the cervical stump in this series raise the still unsettled question of the wisdom of performing total hysterectomy routinely. No matter how one feels about the total operation, it is obvious that, had it been performed in these 29 cases, cervical malignancy could not have developed. The crux of the argument is whether the mortality rate in the hypothetical cases of malignancy in the retained cervix is higher than the absolute mortality of routine total hysterectomy.

(This is an honest and courageous paper, reviewing the past shortcomings in the authors' clinic in a laudable spirit of self-analysis and self-criticism.—Ed.)

POSTMENOPAUSAL ENDOMETRIUM AND ITS RELATION TO  
ADENOCARCINOMA OF THE CORPUS UTERI

G. T. R. FAHLUND AND A. C. BRODERS

Am. J. Obst. &amp; Gynec., 51: 22-38, 1946

The material studied in this paper consisted of postmenopausal uteri in 236 cases. In 86 of these cases the uterus had been removed because of adenocarcinoma and in 100 cases it had been removed for other reasons. In 50 cases routine necropsy had been performed.

In the group of 86 women who had adenocarcinoma of the corpus uteri, all but one had had vaginal bleeding or spotting as a presenting complaint. In these 86 cases there was no appreciable variation in the percentage of cases with proliferative endometrium, whether early or late, or in the percentage of cases with proliferative endometrium, according to the grade of malignancy.

There was no appreciable difference in the percentage of any given type of endometrium in adenocarcinomatous uteri as compared with nonadenocarcinomatous uteri, except with regard to atrophic endometrium. Thus, 41.8 per cent of cases of uteri with malignancy showed atrophic endometrium and only 16 per cent of cases of uteri without malignancy showed atrophic endometrium. This suggests that adenocarcinoma of the uterine corpus is more likely to occur in cases in which there is atrophy of the endometrium than in cases in which there is no atrophy.

Two of the 86 cases of adenocarcinomatous uteri and 3 of the 150 cases of nonadenocarcinomatous uteri presented some features similar to those found in early differentiative endometrium but since they were not entirely the same, the endometrium was classified as late proliferative.

The percentage of cases with grade 3 and 4 cystic change and with grade 3 and 4 accumulation of secretion was roughly the same in the 2 groups of cases. Approximately 42 per cent of the adenocarcinomatous uteri showed no cystic changes, whereas 20 per cent of nonadenocarcinomatous uteri showed no cystic changes. This lends evidence contrary to the view that the "Swiss-cheese endometrium" of Novak has any features predisposing to the development of carcinoma.

There was no consistent difference or variation of cystic change, accumulation of secretion in the glands, density of the stroma in and beneath the endometrial epithelium, involvement of the subbasal glands or sclerosis of the arteries and arterioles, according to the grade of adenocarcinoma. In 28 of the 86 cases no subbasal glands were found. Thus, subbasal glands seem to have no causal relationship to adenocarcinoma of the uterus.

There was virtually no difference in average thickness of endometrium in adenocarcinomatous uteri as compared with nonadenocarcinomatous uteri.

The incidence of endometrial polypi in uteri without adenocarcinoma was roughly 8 times greater than their incidence in uteri containing adenocarcinoma. However, previous curettage in all cases of malignancy might be partially responsible for the variation.

In general, it may be concluded from this comparison of adenocarcinomatous and nonadenocarcinomatous uteri removed from women who had passed the menopause, that the uninvolved portion of endometrium in the former group was in no demonstrable way different from that of the endometrium in the latter group, except that atrophic endometrium was found more often in adenocarcinomatous uteri than in nonadenocarcinomatous uteri, while endometrial polypi were found more often in nonadenocarcinomatous uteri. 7 figures.

(The authors, at the outset of their paper, state that they will not use such terms as "endometrial hyperplasia", "cystic hyperplasia" and "Swiss-cheese hyperplasia", which every gynecologist would understand. Instead of these they choose to employ such terms as "early proliferative with atrophy" and "late proliferative with atrophy" in describing the appearance of the endometrium, and these will seem puzzling, somewhat paradoxical and certainly unfamiliar to most gynecologists and pathologists. It is unfortunate that the authors, in their historical review of previous reports as to the possible relation of hyperplasia and adenocarcinoma, do not always mention whether the hyperplasia was postmenopausal or whether it was the common type encountered during the reproductive era.

This, after all, is a very important point. So far as I know, no one has ever attributed the slightest importance to the latter as a predisposing factor in the development of adenocarcinoma. Certainly there was no such implication in the paper which we published in 1936 and to which the authors refer. It was only in the far less frequent cases of postmenopausal hyperplasia that we noted a not infrequent association with adenocarcinoma, as Taylor had done in 1932, and suggested a possible predisposing relationship. More recently I have published (*Jour. Clin. Endocrinol.*, 4: 575, 1944) another study of the varying histological pictures encountered in the postmenopausal period, including at times typical Swiss-cheese hyperplasia of active and not retrogressive type, though the latter is even more often seen. For that matter, Fahlund and Broders likewise encountered a considerable proportion of proliferative endometria. They say that the proportion was about the same in carcinomatous and non-carcinomatous uteri, which would seem to prove very little one way or another. For example, probably most gynecologists still believe that chronic irritative lesions of the cervix predispose to cancer, but the proportion of women with such lesions and without cancer would probably be hundreds of times greater than those in which these lesions coexist.

As the authors state that all the uteri in their group had been previously curetted, the illustrations included in their paper probably give a less accurate idea of the endometrium in the uninvolved portions of the uterus than if the study encompassed also the tissue which had been curetted away. I have commented on this paper rather fully since our own papers on the subject were referred to by the authors. That adenocarcinoma and postmenopausal hyperplasia or less pronounced proliferative endometria not infrequently coexist permits of no doubt. Whether this is purely coincidental or whether the hyperplasia, presumably estrogen-induced, plays any predisposing role in the development of adenocarcinoma, I am sure I don't know, though I think it possible.—Ed.)

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have not studied the problem in any intensive fashion. I have often seen residual carcinoma, not infrequently in the mucosa itself, after what had apparently been adequate radiation, although the proportion of cases in which such findings are noted will obviously be influenced by such factors as dosage and technique. On the latter point there are still wide variations, and there must be uncertainty in many cases as to whether a lesion which is perhaps localized receives an adequate radium effect. The popular plan at the moment is to follow radiation with panhysterectomy, the interval being ordinarily six weeks. Certainly I would agree with the author that hysterectomy should be a part of the treatment of all cases in which some contraindication is present, such as age, serious disability or organic disease, or a very advanced stage of the disease. Nor would I criticize anyone who, in the occasional early case, proceeds with radical operation without preliminary radiation.—Ed.)

## CARCINOMA CORPORIS UTERI IN 2 SISTERS AGED 34 AND 32 YEARS

ANTHONY W. PURDIE

*J. Obst. & Gynaec. Brit. Emp.*, 52: 575-79, 1945

Two cases are presented of corporeal uterine cancer occurring in sisters aged 34 and 32 years. Both were nulliparae, presenting themselves with the complaint of severe vaginal bleeding. Curettings on both revealed corporeal carcinoma. The diagnosis in each case is substantiated by microphotographs. Total hysterectomy with bilateral salpingo-oophorectomy in one case and left salpingo-oophorectomy in the other (the right ovary had been removed previously) was performed. Both sisters made normal recoveries and have remained well and free from any sign of recurrence.

The largest number of cases of corporeal carcinoma has been found to occur in the postmenopausal age group. However, it is erroneous to state that corporeal uterine carcinoma never occurs before the menopause. The 2 cases presented in this report are not isolated, as is shown by a brief review of the literature. A small but appreciable number have occurred in the 4th decade and from time to time the condition is met with at the age of 19 or 20. It can even occur in childhood, having been found, according to Shaw, in 12 cases of children and adolescents.

The other aspect of the matter is familial occurrence. In considering a familial tendency to cancer, we may be interested in its occurrence in any organ of the body, but the tendency to malignant tumors in one organ in members of the same family is of particular interest. This has been reported by others in mothers and daughters of the same family, the uterus being the organ affected. In the present 2 cases, the mother died of cancer of the rectum and 2 maternal uncles of cancer of other organs. 4 figures.

(While the exact role of heredity in cancer predisposition is still a matter of dispute among the scientists, it would be difficult to persuade any practitioner of long experience

A HISTOLOGIC STUDY OF THE EFFECT OF IRRADIATION  
ON ADENOCARCINOMA OF THE ENDOMETRIUM

LYMAN M. STOWE

Am. J. Obst. &amp; Gynec., 51: 57-66, 1946

In a review of the literature dealing with the detection of residual tumor and its frequency in adenocarcinoma of the endometrium treated with radium, radon and deep x-ray therapy, the author has found that an apparently viable tumor persisted in from 12.5 per cent to 89 per cent of the reported cases. There was wide variation in the amount of therapy given, in the type of radium or radon applicators used, in the intervals between irradiation therapy and operation, and in the thoroughness of the search for residual tumor in the operative specimens.

The uteri of a series of 53 women were studied in this paper and the incidence of residual tumor was found to be 50.9 per cent. All of these patients had intra-uterine radium application; 23 had deep x-ray therapy as well. In a small series in which x-ray was employed in adequate dosage together with radium irradiation, the incidence of residual tumor fell to 40 per cent, while in a longer series where radium alone was used the incidence was 56.5 per cent.

In 46 of the 53 cases a jointed tandem applicator was used. This was designed to overcome the effect of variations in size and shape of the uterine cavity. The uterine cavity is measured directly and 5 capsules containing the radium element are placed in series in a long piece of rubber tubing, the capsules being fixed in position by firmly ligating the tubing between adjacent capsules. The resulting triangle has 2 capsules on each side and one at the base. The applicator will bend to some degree to accommodate itself to varying shapes of the cavity. The practice has been to place in succession in the tubing capsules containing 7, 10, 15, 10 and 8 mg. of radium, respectively. The combined effects of these will produce a diffuse dose to the cavity. In most instances, introduction of this applicator is rapid and simple.

In the majority of instances where residual carcinoma was found, it was seen in the musculature of the uterus. The persistence of viable tumor deep in the muscle might be a consequence of inadequate irradiation of the tissues at even small distances from the source of energy. Also, no evidence has been obtained from this study to suggest that tumor which has involved the muscle to lie beneath the surface is ever destroyed by irradiation.

It is apparent that eradication of adenocarcinoma of the body of the uterus is not attainable by these methods of irradiation therapy. The fact that residual carcinoma was found to be present in the uteri of a high percentage of these patients, even in the most heavily treated group, makes it quite clear that surgical attack must be considered to be the essential feature of curative therapy in the treatment of these cases. It is still possible that preliminary irradiation may be useful as additional therapy or as palliation. 4 figures.

(While the series of cases studied is not very large, the results are not unlike those noted by a number of other authors, or like those encountered from time to time by many of us who

type in the superior lobes of both lungs. The uterus contained a pregnancy of 4 months and the left ovary a large corpus luteum.

Microscopically the pleural tumor revealed very interesting and surprising findings. The epithelial gland structures showed tortuosity and were covered by a single layer of high columnar epithelium, which in some areas presented pluristratification. They showed marked proliferation with many atypical nuclei and some mitotic figures. The stroma was composed of loose edematous tissue containing many vessels, hemorrhages and necrosis. In some areas, however, these connective tissue cells looked exactly like real decidual cells. As a matter of fact, the whole pathologic picture reminded one very much of a hypertrophic premenstrual endometrium with decidual-like reaction. However, no smooth muscle could be seen. The diagnosis of papillary adenocarcinoma of the pleura was confirmed, the growth showing epithelial and stromal changes resembling a decidual reaction.

All three cases present very interesting features bearing on the pathogenesis of endometriosis.

The first one, offering a good example of the rare location of endometriosis on the small intestine, may be explained either by the serosal metaplasia theory of Robert Meyer or as a secondary implantation of endometrium according to Sampson's theory. Peritoneal inflammatory processes considered by many as one of the causes of metaplastic changes on the serosa, were in this case present in great amount. Even more interesting is the extraordinary muscular development that had occurred around the ectopic endometrium, giving rise to a real adenomyoma which caused the intestinal occlusion. According to Speeman's ideas, this process can be explained as the immediate result of a productive or inductive irritation carried out by the epithelial proliferation (endometrial tissue) on the smooth muscle of the intestine.

The last 2 cases seem to demonstrate a susceptibility of the pleural epithelium, under certain conditions, to endocrine stimuli. In fact, the second case showing a real endometriosis of the pleura constitutes a good example of the possibility of direct conversion of the structures derived from the celomic epithelium into endometrial formations, by means of metaplastic changes. As we know, both pleural epithelium and peritoneal endothelium have a common origin from the celomic epithelium, and thereby a genetic relation is maintained with the epithelium of the genital tract. If peritoneal endometriosis can be explained through a process of metaplasia of the peritoneal epithelium, there is no reason why similar changes cannot occur on the pleural epithelium. It is possible that its cells may reacquire embryonic capacity by means of regenerative processes and thereby undergo metaplasia under endocrine stimulants. As a matter of fact this case illustrates the transformation of the pleural epithelium into real endometrium within a chronic, hyperplastic and regenerative inflammatory process. It constitutes a good argument against Sampson's theory, which cannot explain the extra-abdominal occurrences of endometriosis.

The third case represents a very valuable complement to the second one. In fact, the characteristic decidual reaction undergone by the stroma of the malig-

that there are not certain families so heavily permeated with the disease that the factor of coincidence can scarcely be invoked. As to the matter of age incidence, the author is certainly right in emphasizing that a considerable proportion, perhaps a fourth of all cases, of adenocarcinoma occur during menstrual life. We have in our laboratory seen quite a number in the twenties, and in rare instances the disease has been noted even in children.—Ed.)

## CONSIDERATIONS CONCERNING THE PATHOGENESIS OF ENDOMETRIOSIS.(IN RELATION TO THREE CASES OF EXTERNAL ENDOMETRIOSIS)

WALTER BÜNGELER AND DECIO FLEURY SILVEIRA

Arq. de cir. clin. e exper., 3: 169-87, 1939

The authors report 3 unusual cases of endometriosis, one of them unique in the literature. The first is one of an endometrial nodule, the size of a cherry, in the wall of the ileum about 6 cm. from the ileo-cecal valve. The patient was 39 years old. It produced an intestinal obstruction, for which ileo-cecal resection was required. The patient died and autopsy showed extensive pelvic endometriosis.

The second case was that of a 42 year old patient who died with chronic pneumonia. At the autopsy, besides the pleuro-pulmonary lesions characteristic of the disease, there were 3 small round nodules, soft and red, well delimited on the cupola of the right pleura which was very much thickened and partially hyalinized, showing microscopically a fibroblastic pleurisy. The nodules showed a very unexpected but definite picture of endometriosis with typical premenstrual reaction. The glands, tortuous in outline, were surrounded by a very cellular stroma and a compact connective tissue containing a large amount of intracellular hemosiderin. In some areas, encircling the epithelial islands, there was smooth muscle.

The uterus showed a very thickened premenstrual type of endometrium. Within the internal muscular layers there were multiple small foci of endometrial tissue (adenomyosis) which showed also a premenstrual reaction. Both ovaries presented several follicle cysts and the right one a benign papillary pseudomucinous cystadenoma. This case of pleural endometriosis is apparently unique in the literature.

The third case was that of a 37 year-old patient, 4 months pregnant, presenting a specific pleuritis, who had undergone treatment within the last 4 years for a suspected tuberculosis of the right superior pulmonary lobe. For the last 4 months, i.e., since she became pregnant, there had been an increase in the severity of the respiratory symptoms. A puncture biopsy revealed papillary adenocarcinoma, either of the lung or pleura. The patient died 8 days later and at the autopsy, a primary carcinoma was found on the right pleura, with complete encapsulation of the right lung and multiple metastases in the mediastinal, cervical and retroperitoneal glands. There was tuberculosis of the productive

The patient, a 38 year old woman, was first seen with the complaint of mid-epigastric pain, nausea and vomiting. An appendectomy had been performed 14 years previously. The first attack of pain had occurred about one and one-half months before at the time of her regular menstrual period, lasting until the period stopped. During the intermenstrual period and during the next regular period she had no pain. Prior to her admission she started to menstruate again and the same pain recurred. Vomiting brought some relief but the pain persisted for the remainder of the period.

Peptic ulcer and cholelithiasis were ruled out by an upper gastrointestinal series and cholecystogram. Gastric analysis was normal. Antispasmodics and sedation were prescribed during the following intermenstrual period and the patient was without symptoms. During the next menstrual period there was severe lower right quadrant pain, distention, nausea and vomiting. A gastrointestinal series with barium enema established the diagnosis of small bowel obstruction.

At operation the terminal ileum showed what appeared to be a hard constricting band of fibrous tissue about 3 inches from the ileocecal junction, completely occluding the lumen of the bowel. A resection of the involved portion was done with a side to side anastomosis of the ileum and cecum. The histologic diagnosis was endometriosis of the ileum.

(As the authors state, it is generally the sigmoid or rectum which is involved in intestinal endometriosis, but at times the terminal ileum or appendix may be a site of the disease since these are often located in the true pelvis, to which endometriosis is almost entirely confined. However, intestinal endometriosis may occasionally occur in the entire absence of pelvic endometriosis. For example, in the course of a hysterectomy for myoma some time ago, a hard, freely movable mass was accidentally noted in the ileum, simulating an annular carcinoma. The patient had had no obstructive symptoms but x-ray studies shortly after her operation confirmed the presence of an organic lesion thought to be carcinoma. A resection was done, but microscopic examination showed endometriosis instead of cancer. In this case there was no endometriosis in the ovary or elsewhere in the pelvis. See also comment on preceding paper.—Ed.)

## ANGIOMA OF THE UTERUS

LÉVY-SOLAL, BRET AND DUPERRAT

Gynéc. et obst., 44: 332-34, 1945

The case is presented of a 40 year old woman whose menses had been normal until November 17, 1944. The flows which occurred on December 9th, 15th and 23rd were blackish and contained some clots. At these times the patient had intense hypogastric pains, paroxysms, nausea and dizziness. The bleeding of December 23rd lasted 14 hours. The patient's general condition had altered and she had lost 4 kilograms.

nant tumor in the coexistence of pregnancy, besides its epithelial changes, can be explained as the result of a sensibility acquired by the pleural neoplastic tissue (embryonic characteristics) to the endocrine stimuli of gestation.

(A considerable group of cases of intestinal endometriosis, often producing obstruction and requiring colostomy or resection, have been reported. The rectum and sigmoid are naturally the portions of the bowel most frequently involved. In extensive pelvic endometriosis, the rectal or sigmoid wall may show such massive infiltration as to simulate carcinoma perfectly, and this mistake has been frequently made, especially by general surgeons not familiar with the vagaries of endometriosis. Unless obstruction has actually occurred, the complete removal of ovarian tissue is all that is required to relieve the patient, since the aberrant tissue then retrogresses, its shrunken residua usually causing little or no discomfort to the patient. No longer is there any justification for the extensive and hazardous resections at one time advocated and practiced for such bowel involvement unless, as already mentioned, complete obstruction has already occurred.

The second case, that of what appears to have been a genuine pleural endometriosis, is of great interest and, as far as I know, is actually unique in the literature. Whether the explanation offered by the authors is correct must of course remain a question. Only certain "celomic zones" appear to be favorable to the development of endometriosis, such as the pelvic peritoneum and segments of the anterior parietal peritoneum. The upper abdominal peritoneum seems to be practically immune. The other possible explanation, not mentioned by the authors, is that of hematogenous dissemination of endometrial tissue. This, for example, is the only possible explanation in the few reported freak cases of what was apparently genuine endometriosis in such locations as the upper arm or thigh. The experimental work by Hobbs shows that in cats endometrium introduced into the blood stream grows quite readily in the lungs. These experiments are at least suggestive in attempting the explanation of pleural endometriosis.

The third case must, I think, be viewed with some skepticism. This patient had a very definite papillary carcinoma and one would have to lean backward from interpreting certain histological features of this growth as representing instances of ectopic decidual growth. This statement is made simply because all sorts of gradations of gland and stromal changes in adenocarcinomata of the type described by the authors are possible and might, at times, simulate decidua. On the other hand, it is possible that an examination of the slides or of good photomicrographs might incline one to agree with the authors that the existing pregnancy in their third case had actually elicited a decidua-like response in parts of the tumor which they describe.—Ed.)

## ENDOMETRIOSIS CAUSING INTESTINAL OBSTRUCTION.

O. T. WOOD, I. DEIBERT AND T. KAIN

J. A. M. A., 130: 341-43, 1946

The general incidence of endometriosis has been reported as 8.9 per cent in 1000 surgical cases. Intestinal obstruction, as a result of endometriosis, has been observed frequently but most instances are those involving the sigmoid and the mesorectum. Relatively few cases of acute complete obstruction have been recorded. The authors present the following case as being of interest because of the short duration of symptoms from the time of onset.

diagnosis had been made of myomas of the uterus. A subtotal hysterectomy was done with unilateral salpingectomy and bilateral partial oophorectomy. The pathological report was multiple fibromyomas of the uterus, myosarcoma of a submucous fibroma and lutein cyst of an ovary. About 8 months prior to the present admission she developed pain in the left knee when standing or walking. A roentgenogram of the left knee and hip showed an abnormal process consisting of diffuse erosion of the head of the femur. The patient failed to return to her physician but consulted a chiropractor until the pain involved the left hip and was so severe that she could not get out of bed one morning.

At the present admission, films of the left hip showed a fracture involving the neck of the left femur with some apparent erosion and rarefaction of the neck of the femur. This was thought definitely to be due to a pathologic fracture resulting from bony metastasis. A biopsy of the femur at the fracture site showed interlacing bundles of spindle-shaped cells. Irregular pyknotic masses of nuclear substance were observed in large numbers, but comparatively few clearly defined mitotic figures were seen.

The biopsy wound became infected and in spite of treatment, the patient died. The anatomic diagnosis was leiomyosarcoma of the uterus with extension to the pelvis, abdomen and left femur. 7 figures.

(Sarcoma may arise not only in myomas, but in any of the tissue elements of the uterine wall. Some cases, including many arising in myomas, are of a relatively low degree of malignancy, but others, especially many of the intramural or endometrial group, are highly malignant. Unlike the carcinomas, recurrence is not regional in the pelvis, except where removal has been incomplete, but occurs to distant organs, as the authors mention. For this reason, there is no rationale for postoperative irradiation of the pelvis if a complete operation has been done. I have seen two instances of sarcoma metastasis to the brain.—Ed.)

## HYPERTROPHY OF THE UTERUS

ARTHUR H. CURTIS

Am. J. Obst. & Gynec., 50: 748-52, 1945

Hypertrophy of the uterus is characterized by morbid enlargement or overgrowth, particularly of the body of the uterus. The uterus is symmetrically enlarged and heavy, the uterine walls thickened and the cavity enlarged beyond its normal capacity. The endometrium varies; it may be entirely normal or it may be thickened or even polypoid if there is hormonal imbalance or obstructed uterine drainage. Associated numerous and varied changes may be present in the cervix, Mackenrodt's ligaments, ovaries and other pelvic tissues, dependent upon the etiology of the hypertrophy and the severity and duration of the condition.

The author classifies hypertrophy of the uterus as follows: (1) Chronic sub-

A pelvic examination on January 2nd revealed no abnormalities; the uterus was small, anteverted and inflected to the left; the adnexa were normal. The currettings and smears appeared to be normal. On January 4th, a lipiodol examination was made. The plates revealed a filling defect of the left horn of the uterus. After total hysterectomy, examination of the left horn showed a small, hard, brownish mass, the size of a lentil, which obliterated the uterine ostium. Histological examination revealed this mass to be composed of fibrin, erythrocytes and neocapillaries. It was clearly a well developed fibrino-cruoric blood clot. The mucus below it had disappeared and the clot was implanted directly on the angiomatous tissue from which it arose. The inner stratum of the myometrium was hollowed out by small winding cavities which were lined with a slight, single endothelial coating with clearly defined nuclei. In some places it was filled with blood. A diagnosis of capillary angioma of one of the walls of the uterine horn with a fibrino-cruoric surface clot was made. The hemorrhagic manifestations were interpreted as sequelae to an ulceration process on the surface of the angiomatous region of the uterus, and the organized clot was presumed to be a manifestation of the healing process. 1 figure.

(While angiomas of the uterus occur, they are exceedingly rare. The description given by the authors seems to justify their designation of the small growth as an angioma; and photomicrographs are not available for comment.—Ed.)

## LEIOMYOSARCOMA OF THE UTERUS WITH METASTASIS TO THE FEMUR; REPORT OF A CASE AND REVIEW OF THE LITERATURE

W. S. BROOKE AND J. R. THOMASON

Arch. Surg., 51: 120-24, 1945

Sarcoma of the uterus is a rare neoplasm, probably occurring in not more than one per cent of patients who are operated on for uterine fibromyomas. The condition may be encountered in children but it is more common in women in the menopausal period, especially during the 5th and 6th decades. It is not certain whether the tumor arises primarily or whether it develops from a pre-existing fibroid. The number of mitotic figures is usually an index to the degree of malignancy.

Metastases from sarcoma of the uterus are most common in the lungs, peritoneum, lymph nodes, liver and kidneys. Little has been written concerning metastases of uterine sarcomas to bone. The authors were able to find only 3 cases reported and they know of one questionable case through personal communication. The following case is presented, in which metastasis occurred in the femur.

The patient, a 43 year old woman, was admitted to the hospital complaining of pain in the left hip of 8 weeks' duration. Several years previously an operative

## THE ADNEXA

### DERMOID CYSTS OF THE OVARY: THEIR CLINICAL AND PATHOLOGICAL SIGNIFICANCE

W. J. BLACKWELL, M. B. DOCKERTY, J. C. MASSON AND R. D. MUSSEY

*Am. J. Obst. & Gynec.*, 51: 151-72, 1946

Believing that a review of a large group of cases of ovarian dermoid cysts might produce some valuable information, the authors undertook the present study. Answers were sought for such questions as these: what are the usual histologic components of the tumors and how many tumors are truly monodermal? Are the symptoms and signs produced diagnostic of the tumor type? What is the incidence and what are the types of malignant transformation seen in ovarian dermoids?

With the exception of an article by Pauly in 1875, a review of the literature shows a surprising lack of historical material on this important subject. The data obtained from an extensive review of the writings show that these cysts have been reported to contain a variety of substances: namely, hair, teeth, bone, nerve tissue, smooth muscle fibers, bone connected by a false joint lined by periosteum, well developed mammary glands, tissues resembling cecum and appendix, thyroid tissue, corpus luteum cysts in the walls of dermoids, an adrenal, a lens and eyelid, salivary glands and a rudiment of lung.

The large number of hypotheses which have been advanced to explain the origin of these tumors is evidence that knowledge concerning their cause is still conjectural. Currently the most discussed hypotheses are misplaced blastomere and parthenogenetic development of ovum.

The conclusions presented in this paper were drawn from a study of the data obtained from the records of 225 patients who had cystic teratomas removed surgically at the Mayo Clinic and from microscopic examination of 100 consecutive tumors from this group.

The incidence of dermoids is usually stated to be about 10 per cent of all ovarian neoplasms, but the incidence of this series was only 5 per cent. The tumors occurred with equal frequency in either ovary. Twelve and four-tenths per cent were bilateral. The patients' ages ranged from 7 to 72 years; approximately 85 per cent of the tumors were removed from patients between the ages of 16 and 55 years. It was believed that those removed from older patients had arisen before cessation of ovarian activity.

Gross examination revealed that the tumors were soft and cystic at body temperature unless they contained bone, cartilage or teeth. The oily content of the cysts was composed of fat, desquamated epithelium, glycerides of fatty acids, cholesterol and other alcohols. From the inner surface of the wall there usually projected a white shiny protuberance to which numerous hairs were attached.

involution, which presents an exaggeration of normal physiologic function either with or without infection. It is chiefly ascribed to an endocrine factor. (2) Diffuse hypertrophy, which may be cited as an example of chronic subinvolution, where the uterus is massive, hypertrophic and badly retrodisplaced. This type presents a proportionate increase in the various elements of the uterine wall, i.e., overgrowth of muscle, the connective tissue and the blood vessels. (3) Chronic metritis, in which there is a grossly evident infection of the tubes, ovaries or pelvic cellular tissues, histological examination of the uterus presenting the usual residual evidence of an inflammatory process.

The usual symptoms are prolonged or excessive menstruation, pelvic pressure with aching discomfort and increased vaginal discharge. Differentiation from carcinoma of the uterine body is sometimes difficult. Histologic diagnosis of the various types of uterine hypertrophy is facilitated by differential stains. Various gradations of hypertrophy are encountered in most instances and pure subinvolution or true diffuse hypertrophy or hypertrophy due solely to metritis or to endocrine disturbance is unusual.

Curettagé, a diagnostic procedure in these cases, may also prove beneficial at times. If more important surgical intervention is required, corrective operations for displacement should be considered only if childbearing is an important issue; subtotal or complete hysterectomy is the procedure of choice. 4 figures.

(A paper by Williams and Kinney, published 2 years ago (*Am. J. Obst. & Gynec.*, 47:380, 1944) contained the suggestion that the term "myometrial hypertrophy" be used in lieu of such terms as fibrosis uteri, chronic metritis, arteriosclerosis uteri and metrorrhagia myopathica, and Curtis makes essentially the same suggestion in the paper abstracted above. If the author proposes to use the term hypertrophy as a mere synonym for enlargement, there can scarcely be any objection to it as a loose clinical designation. As he says, many factors may be concerned in bringing about such an enlargement, and he himself enumerates a number of these, such as subinvolution and chronic metritis. It is perfectly true that there has been much floundering in the use of such designations as fibrosis uteri, chronic subinvolution, chronic metritis and diffuse hypertrophy. In some cases such terms can be intelligently applied; in others there will be uncertainty and confusion. But certainly no laboratory of gynecological pathology would wish to dump them into a general category designated as hypertrophy.—Ed.)

ovary measuring 7 by 7 by 6 cm. Several small, thin-walled translucent cysts were noted in the cortical zone of normal ovarian tissue. Microscopic examination disclosed the mass well-demarcated from a thin zone of normal ovarian tissue. The latter contained several simple follicular cysts which were visible in the gross specimen. A moderate-sized cystic area was noted within the neoplastic mass. The cyst cavity contained a papillomatous structure, whose stroma had a myxomatous appearance. Stains for phospholipids were positive and foot silver stains revealed an abundant reticulum. The final diagnosis was theca-cell cystoma.

The gross specimen in the second case consisted of a large nodular uterus, both normal-appearing Fallopian tubes and a small right ovary. A large cystic mass was noted arising from the left adnexa, firmly adherent to the left lateral aspect of the uterus. On section the mass was multilocular. There were several large cyst cavities and many small cysts. Microscopic examination revealed the dense fibrous areas formed of spindle-shaped cells of fibroblastic appearance. The thin walls of the cystic locules were formed of similar cells. Stains for phospholipids were positive and foot silver stains revealed an abundant fine reticulum. The final diagnosis was theca-cell cystoma.

The observation of cyst proliferation in this type of tumor, heretofore only reported as solid tumors, lends support to the theory advanced by Novak, Traut and others that these tumors arise from early ovarian mesenchyme. The author calls attention to the fact that these tumors may reach such large proportions as to be readily confused with other ovarian cystomas. 6 figures.

(Thecomas as a group do not reach the large size attained by many granulosa cell tumors and they are commonly solid. In the first of the 2 cases reported in this paper, the illustration shows a lining of a single layer of granulosa cells, suggesting that a simple follicle cyst might be coexistent with the thecoma. Such an explanation would scarcely apply to the very large cyst in the case, and the description of this tumor would suggest that it is of granulosa thecomatous nature. With granulosa cell tumors, especially those of large size, cyst formation is of course relatively common.—Ed.)

## GRANULOSA-CELL TUMOR WITH PREGNANCY FOLLOWING REMOVAL

J. E. AYRE AND W. R. FOOTE

Am. J. Obst. & Gynec., 51: 260-64, 1946

The granulosa-cell tumor makes up about 2 to 3 per cent of all solid ovarian tumors. It appears most commonly in women about the menopausal age but occasional examples are seen in young women between puberty and the menopause, while a few have been observed in children.

During the period of sexual activity the symptomatology due to the endocrinal potencies of the tumor is less noticeable than at other ages because of the proximity of normal menstrual function and also because the other ovary,

The protuberance frequently was covered with hair and contained cartilage, bone and teeth. In this series, teeth were present in 31 per cent of the cases. It was observed that the tumors are of slow growth and that the average size is 8.2 cm.; bilateral tumors average 7.75 cm. in diameter.

Microscopic examination revealed that ectodermal derivatives were present in 100 per cent of the tumors, mesodermal structures in 93 per cent and entodermal derivatives in 71 per cent of these cysts. The high percentage of mesodermal and entodermal elements was due to the fact that multiple sections were examined. Serial sections probably would have revealed more.

The authors believe that the term "dermoid cyst" does not fully define nor describe the growth. Since all embryonic layers may be represented, the authors suggest that these cysts should be regarded as teratomas and that they should be designated as cystic teratomas.

The hypotheses that have been advanced to explain the histogenesis of these neoplasms do not adequately explain their origin. Malignant lesions occurred in 3 per cent of cystic teratomas. Symptoms associated with these cysts had no differential diagnostic value. Surgical removal was the treatment of choice but, when possible, resection of the tumor was done to conserve ovarian function. 8 figures.

(The Section on Pathology of the Mayo Clinic has been very assiduous in recent years in reviewing the large gynecological material at its disposal, and has thus made a number of valuable contributions, especially in the statistical study of ovarian tumors. The present paper, based on 225 cases, is of interest chiefly in emphasizing the endless variations in the histological components of dermoid tumors. Even an expert histologist will often find it difficult to identify some of the elements that may be encountered. The authors find the incidence of dermoids to be much less than that generally given of 10 per cent of all ovarian neoplasms, and I would be inclined to believe that their figure of 5 per cent is more nearly correct. I agree with them also that the term cystic teratoma would probably be a better one as applied to the so-called simple dermoid cyst. However, the way of the reformer in medical nomenclature is a pretty hard one, and it will probably be as hard to dislodge the term "dermoid cyst" as it would be to abolish the use by gynecologists of the term "fibroids" in speaking of uterine myomas.—Ed.)

## THECA-CELL CYSTOMA OF OVARY

J. G. SHARNOFF AND J. R. LISA

Am. J. Obst. & Gynec., 51: 253-59, 1946

Cyst formation, observed in a few cases of theca-cell tumors of the ovary, has been attributed to liquefaction necrosis of the neoplastic tissues. In the past 6 years, of a total of 10 theca-cell tumors observed by the authors, 2 cases were studied which warranted their designation as theca-cell cystomas. In both instances cyst proliferation was noted.

The gross specimen in the first of these cases was that of a markedly enlarged

ovary measuring 7 by 7 by 6 cm. Several small, thin-walled translucent cysts were noted in the cortical zone of normal ovarian tissue. Microscopic examination disclosed the mass well-demarcated from a thin zone of normal ovarian tissue. The latter contained several simple follicular cysts which were visible in the gross specimen. A moderate-sized cystic area was noted within the neoplastic mass. The cyst cavity contained a papillomatous structure, whose stroma had a myxomatous appearance. Stains for phospholipids were positive and foot silver stains revealed an abundant reticulum. The final diagnosis was theca-cell cystoma.

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During the period of sexual activity the symptomatology due to the endocrinal potencies of the tumor is less noticeable than at other ages because of the proximity of normal menstrual function and also because the other ovary,

often normal, may serve to mask the picture. However, there is usually a period of amenorrhea or there may be simple irregularity of the menses. In the amenorrheic stage there may also be an associated hirsutism.

Approximately 80 per cent of the granulosa-cell tumors are clinically benign. When malignant, they metastasize rapidly. In a young woman, following removal of a benign granulosa-cell tumor, fertility should not be unexpected unless both ovaries have been removed.

The author presents the case of a 35-year-old woman with a palpable pelvic tumor and associated lower abdominal pain. From the menarche, at 13 years of age, intermittent amenorrhea was noted, menstruation occurring at intervals of 6 weeks to 6 months. Two years after marriage she became pregnant and was delivered of a healthy child. Only one period occurred 4 months after delivery and for the next 4 years the patient complained of amenorrhea, fatigue and nervousness. Gradually she developed a nagging pain in the right lower quadrant and examination revealed a tumor replacing the right ovary.

At operation, the tumor was removed and the left ovary was found to appear healthy. In view of the patient's age and desire to rear further offspring, only the diseased organ was removed. Postoperatively the patient menstruated only once before becoming pregnant. She gave birth to a healthy child and since delivery has had a normal 28-day menstrual cycle and enjoyed her first good health since the onset of puberty. It was of interest that, prior to operation, she was quite nervous and lacked any sexual libido. Since operation she has recovered from the confused state and her sexual desires have been normal.

In this case it appeared that the removal of the conflicting endocrine force permitted rapid physiologic resumption of the normal sexual cycle. It would appear that conservative surgery is justifiable in sparing the second ovary when free from signs of malignant disease in a woman in the reproductive age.

(As the authors state, there is no reason why patients with granulosa cell tumors should not conceive after the removal of the growth, and they refer to a number of instances of this sort in addition to their own case. I agree with them that conservative surgery is justified if one recognizes the granulosal nature of the lesion in younger patients in whom the desirability of preserving the reproductive function is important. However, in most cases the surgeon is likely to consider such tumors to be the more common and more deadly forms of ovarian cancer, especially when the tumor is large and presents as a solid or partly cystic mass. The diagnosis in such cases is more likely to be made in the laboratory than at the operating table. This may be just as well, for in this type of tumor the hazard of later recurrence is a very real one.—Ed.)

## PRIMARY CARCINOMA OF THE FALLOPIAN TUBES

K. A. LOFGREN AND M. B. DOCKERTY

Surg., Gynec. & Obst., 82: 199-206, 1946

Primary carcinoma of the fallopian tube is a rare condition which accounts, in the authors' experience, for only one out of every 625 carcinomas of the female

genital tract. For the most part it is a disease of the menopause and has not been reported among individuals in their prepuberal years.

Symptoms are insidious in their onset with vaginal discharge, pelvic pain and abdominal tumor representing the cardinal symptoms which, however, rarely lead the physician to a correct preoperative diagnosis. The evolution of the disease is more rapid than is indicated by its symptomatology and the majority of patients so afflicted demonstrate lesions of doubtful resectability at the time of surgical exploration. The appearance of the lesion on gross inspection is sometimes deceiving since it may mimic closely familiar conditions of an inflammatory nature. Because of this, every distended fallopian tube should be opened before it is removed from the operating room.

Treatment of these carcinomas, whenever found, regardless of any apparent state of encapsulation, should consist of total abdominal hysterectomy with bilateral salpingo-oophorectomy in addition to removal of any discernibly involved regional lymphatic nodes and peritoneal implants. Postoperatively, roentgen therapy should be administered. In spite of these measures the number of 5 year cures is disappointingly small.

Pathologists who are unfamiliar with the condition will often have difficulty establishing the primary nature of the lesion and should remember that the fallopian tubes are frequently involved in metastasis from ovarian and uterine sources. Actual involvement to the tubal mucosa, strict confinement to the fallopian tube, a marked disproportion between the size of the tubal and extratubal lesions as well as a working knowledge of the histologic pictures of primary uterine, tubal and ovarian carcinomas will be helpful in deciding the primary source in doubtful cases. The epithelial hyperplasia associated with tuberculous salpingitis should be kept in mind and the diagnosis of tubal tuberculosis and carcinoma should not be made except when malignant neoplasia is manifestly indicated. 7 figures.

(As the authors state, primary tubal carcinoma is exceedingly rare, far more so than the secondary variety which may occur with either primary ovarian or corporeal carcinoma. In its advanced stage the disease is commonly bilateral and the tubes may appear as large, rather thin-walled pyosalpinges which often are quite freely mobile, unlike the extensively adherent pyosalpinges of gonorrheal type. The very unfavorable prognosis is due in part at least to the fact that the disease has usually reached a late stage before it gives rise to any worthwhile symptoms. Mitchell and Mohler last year reported the lucky find of a tiny primary carcinoma in the small segment of tube removed at a Madlener sterilization operation (See February Survey, p. 127), and it will be interesting to follow her subsequent course after the complete operation which was done. Dr. Mohler has recently informed me that thus far the patient is apparently free of any recurrence.—Ed.)

BRIEF CONSIDERATIONS CONCERNING TWO CASES OF ACUTE  
TORSION OF THE FALLOPIAN TUBE

RICARDO LOPEZ MONTI AND ENRIQUE VALLAZA

An. d. Inst. matern. y asist. social, Buenos Aires, 6: 90-96, 1944

The literature reports comparatively few cases of acute torsion of the tube. It is hard to conceive how an organ suspended by such a large, wide and thick meso may occasionally undergo torsion, sometimes of several twists, leading even to its amputation in some instances. In the majority of cases, the tube presents some sort of abnormality, such as hydrosalpinx and hematosalpinx, or it coexists with a tumor in either one of the ovaries or even a myoma of the uterus.

The torsion generally occurs following exercise, dancing, etc., and in most cases it is associated with acute symptoms (sharp abdominal pain, tachycardia, etc.), although in other instances the clinical picture is more moderate, the pain being localized on one side or other of the lower abdomen. Usually there is no fever and on pelvic examination one finds an elongated tumor, sometimes cystic in feel, tenderness in the cul-de-sac and frequently an associated ovarian cyst or uterine myoma.

Differential diagnosis must be made from acute adnexitis, tubal pregnancy, torsion of subserous pedunculated myoma, acute appendicitis, perforated cholecystitis and perforated gastric ulcer, mainly from the 3 latter, in order to enable one to choose the adequate operative incision. Although preoperative diagnosis can be made in some cases with the aid of the data furnished by the history, physical examination and laboratory findings, acute torsion of the tube is generally diagnosed at the operating table.

None of the various theories proposed to explain tubal torsion is satisfactory. According to the authors, it seems likely that several factors (lack of tonicity of the abdominal tissues, traumatism, differences of pressure in the pedicle vessels, intestinal peristalsis, etc.) with the predominance of one of them at a certain moment, would give rise to the clinical picture described.

The authors report 2 cases which they had the opportunity of studying.

The first was in a 44 year old patient who complained of acute pain in the right lower abdominal quadrant for 4 days. She had had 2 similar attacks 7 and 4 months before, simulating appendicitis. A laparotomy was performed and the right tube, presenting a hematosalpinx, was found to show a torsion of 4 twists, with complete auto-amputation at the isthmic level. The left tube showed a hydrosalpinx and the uterus a large myoma. Both ovaries were normal. A bilateral salpingectomy and supravaginal hysterectomy were performed, followed by uneventful recovery. The number of twists presented by this tube constitutes an interesting finding.

The second case was that of a 48 year old patient who complained of right abdominal pain for 9 days, almost simulating an acute attack of appendicitis. The laparotomy showed a dermoid cyst of the left ovary, the size of a large

orange, fixed to the cul-de-sac with the corresponding tube. The right adnexa were entirely adherent to the cecum. Following dissection of the adhesions, the ovary seemed to be normal but the tube presented a hematosalpinx 3 to 4 cm. in diameter. It had undergone torsion at the isthmic portion which showed strangulation and a tendency towards atrophy. Right salpingectomy and left ovariectomy were performed, followed by uneventful recovery. In this case the authors are inclined to believe that the dermoid cyst of the left ovary, by pressure against the posterior surface of the uterus, had contributed to produce the torsion of the tube.

(It is worth remembering that in rare instances even an entirely normal tube may undergo torsion. I have seen 3 patients in whom operation done for other elective indications, and in none of whom previous operations had been done, revealed what at first sight would have been thought to be congenital absence of one tube and ovary. It would be difficult to explain such an anomaly embryologically, in view of the very different embryological "anlagen" of the tube and ovary. Moreover, in each of these 3 patients there was a short stump of tube, resembling the stump of a tube long after resection. Such a picture is explained by the fact that the tubes, with the ovarian ligament, had undergone torsion long before, perhaps even in fetal life, twisting themselves off completely, with later absorption of the organs. Such absorption after torsion and auto-amputation of even large tumors has been observed in at least a small group of recorded cases.—Ed.)

## ARRHENOBLASTOMA

LICINIO H. DUTRA

Med. cir. farm., No. 115, 616-28, 1945

A case of arrhenoblastoma, constituting the 7th in the Brazilian literature, is presented in this paper. According to the author, it presents 2 main points of interest: (1) A high degree of malignancy, a characteristic rarely observed in this type of tumor. In fact, from 70 cases collected from the literature by Krock, 8 were found to be carcinomatous in nature, 9 sarcomatous and 2 mixed. (2) It also demonstrates that the masculinizing symptoms do not necessarily manifest themselves by somatic changes. As a matter of fact, they can be limited to psychic changes, and may not be present at all.

Case report: The patient, aged 52, Japanese, married, was first seen on July 19, 1942 complaining of a large growth within her lower abdomen for the last year. Despite its great size it had never caused her any trouble whatsoever. She was brought to the hospital because of severe pain in the abdomen developing soon after she had suffered an accidental fall. Menarche had occurred at the age of 15. Her menstrual periods used to occur at intervals varying from 30 days to 3 months, were of 3 days' duration, normal flow, and with dysmenorrhea. However, 21 years later they became entirely normal and thus remained until 6 months ago when she developed amenorrhea lasting up to the present time.

There had been one child 23 years ago, the patient never again becoming pregnant.

The history revealed remarkable psychic changes tending toward masculine ideas with complete loss of libido since the onset of the growth. There had been no change in the voice nor evidence of somatic alterations.

On examination the patient was found to be healthy with the subcutaneous tissue normally distributed and developed. There was no abnormality in hair distribution, which was scanty. The abdomen showed a firm tumor in the hypogastric region, the size of an adult's head, round, smooth and arising from the pelvic cavity. After pelvic examination a diagnosis of solid tumor of the ovary or uterine fibroid was made. No signs of masculinization could be found.

Laparotomy was performed on August 8, 1942, and a big, solid, whitish, pedunculated tumor, with torsion of its pedicle, was easily removed from the left ovary. The other genital organs were otherwise normal. The tumor measured 17.2 x 15.5 x 14.6 cm., was covered by a capsule and on cross section it showed a homogeneous structure, without cavities, and was friable and congested.

Pathology: "Arrhenoblastoma, atypical form". It showed characteristic epithelial cords with many mitotic figures, and in some areas, large cells with clear, vacuolated cytoplasm and central nuclei, resembling the Leydig cells or the cells from the reticular portion of the adrenal cortex.

Convalescence was uneventful and the patient refused to have x-ray treatment. She remained well for the following 6 months and her marital life became normal but the amenorrhea persisted. Symptoms of recurrence then appeared but the patient still objected to further treatment. On September 8, 1943, almost one year after operation and following an unsuccessful course of x-ray treatment, an exploratory laparotomy was performed. Neoplastic masses were seen growing throughout the entire abdominal cavity, involving the intestines and thus making it impossible to identify the internal genital organs. A biopsy of the neoplastic tissue was then performed and it was microscopically diagnosed as a recurrence of the previous tumor removed.

The patient died on October 10, 1943 in extreme cachexy, with the neoplastic growths extending throughout the abdominal cavity. This particular case illustrates the remarkably malignant character of arrhenoblastoma in some cases. This is the first reported instance in Brazil of arrhenoblastoma with recurrence and metastasis.

(It is certainly possible for an arrhenoblastoma to be present with no symptoms of masculinization. Rather curiously, this has been true in most of the small reported group of the highly differentiated or testicular adenoma types of arrhenoblastoma. As a matter of fact, the unripe and intermediate types appear to have a much more profound biological effect than is seen in the ripe variety. A considerable group of cases is now available in the literature to indicate that arrhenoblastoma is always to be looked upon as potentially malignant, and that recurrence is not infrequent. The endocrine effects of these tumors are often so striking that most cases have been reported rather promptly after their observation, so that evidence of their subsequent course has not been available. It will probably be a good many years before we can form any reasonably accurate estimate of the degree of malignancy of this neoplastic form.—Ed.)

## A CASE OF MEIGS'S SYNDROME

NASID EREZ

J. Obst. &amp; Gynaec. Brit. Emp., 52: 506-07, 1945

The presence of ascites, hydrothorax and an ovarian fibroma is well established as Meigs's syndrome. Thus far the total number of cases recorded, including the one described in this report, is 42.

A 26-year-old woman was admitted to the 2nd University Obstetric Clinic in Istanbul complaining of abdominal swelling and breathlessness which had started 9 months before. She had been treated for pleurisy in the previous winter. Menstruation had always been regular. This patient had cyanosis of the face and dyspnea. The heart was shifted to the left and there was a right pleural effusion. The abdomen was distended with fluid and in the hypogastrium was a hard and irregular tumor the size of a fetal head. The uterus was felt normal in size but lying behind the tumor. The diagnosis was a solid tumor of the ovary with ascites—fibroma or carcinoma. The pleural effusion was considered to be an aftermath of the attack of pleurisy during the previous winter.

Conservative treatment was advised by the internist. Repeated aspirations of fluid from the pleural cavity were followed by reversal to the old fluid level. In view of the persistence of effusion, marked dyspnea and orthopnea, a laparotomy was performed. Prior to operation 2750 cc. of fluid were aspirated from the pleural cavity. At operation an ovarian tumor and 2 litres of blood-stained fluid were removed.

Pathological diagnosis was fibroma of the ovary. The postoperative course was uneventful and at 8 months after operation, a radiograph showed the pleural cavity free of fluid and the level of the diaphragm normal.

The theory is supported that the pleural effusion results from back-pressure in the azygos system. 4 figures.

(The explanation of the hydrothorax in these cases is not yet clarified. A good discussion of this subject is to be found in the article by Rubin, Novak and Squire in *Am. J. Obst. & Gynec.*, 48: 601, (Nov.) 1944. While the syndrome was originally linked up characteristically with fibroma, it has been reported also with other types of ovarian tumor, such as Brenner tumor, thecoma and carcinoma (without pleural metastasis).—Ed.)

## NEOPLASMS IN APPARENTLY NORMAL OVARIES

THEODORE CIANFRANI

*Am. J. Obst. & Gynec.*, 51: 246-52, 1946

The object of this paper is to emphasize the possible occurrence of neoplasms in apparently normal ovaries and to show that some of them can be detected at

operation. Of approximately 1500 normal-appearing ovaries, the following tumors were found: 3 dermoids, one Brenner tumor, one fibroma, one papillary cyst adenocarcinoma, and one granulosa-cell tumor. Two of these were discovered through routine pathologic examination of ovaries removed at operation and the other 5 were found by examination of the ovary during operation. These small neoplasms ranged in size from a few millimeters to 1.5 cm.; none of the ovaries that harbored them was more than average size. Though they were mere infant growths when discovered, such tumors eventually would have enlarged, but their early discovery and removal averted serious consequences.

Brief case histories and microphotographs of the 7 tumors are presented.

The author suggests that if the many clinics in this country in which abdominal operations are done made a special effort to examine, with extreme care, all normal-sized ovaries, the percentage of positive findings of pathology in normal-sized ovaries would be equalled if not exceeded. Careful examination should include inspection, careful palpation for areas of abnormal consistency, and if necessary aspiration with a needle. Even incision may be done with no harm in suspicious cases. The routine puncturing of small follicle cysts for the purpose of diagnosis is recommended. Special attention should be given to the normal ovary in patients operated upon for unilateral ovarian growths. 7 figures.

(The author is to be commended for urging the meticulous examination of ovaries at operation as well as in the operating room, even though the yield of unsuspected early neoplasms in normal-appearing ovaries may not be as large as his paper implies. The surgeon who knows something of pathology is apt to exhibit an operating room technique quite different from that of his colleague who is interested chiefly in the merely mechanical procedures of the operation. The former will be likely to note even such physiological features as corpora lutea or atretic follicles and try to correlate the ovarian picture with the menstrual phase of the patient; he will note even small nodules or outgrowths on any of the pelvic organs, for they may be of great pathological interest; he will usually, even though it may spoil the gross beauty of the specimen, wish to see the inside of ovarian cysts as soon as they are removed, as this may give him information as to possible malignancy which may not be evident by external examination; he is likely to cut into even normal looking ovaries if they have been removed, for their physiological as well as possible pathological interest; he is apt himself to cut out blocks showing endometrial "implants," since he knows that these may lose their conspicuousness when the tissue is fixed, and may thus be missed in routine laboratory examinations; he will want to see the inside of the uterus before the abdomen is closed, and thus avoid the occasional postoperative regrets at an overlooked malignancy; and above all, he will not consider that his study and management of any case is complete until he has followed the sections through the laboratory. Does this sound utopian? I do not think so, for a larger and larger proportion of our gynecologists, especially the younger generation, are doing just this, and getting a lot more fun out of their work than they would otherwise. It is just this interest in pathology which, more than any other one thing, is likely to spell the difference between a real gynecologist and a mere gynecological surgeon.—Ed.)

A CASE OF OVARIAN SEMINOMA IN A CHILD OF TEN  
AND A HALF YEARS

ROBERT DUPONT

Mem. Acad. de chir., Paris, 71: 100-02, 1945

The patient whose case is reported in this paper was admitted to the hospital at the age of 10½ years because of sudden, acute abdominal pain accompanied by vomiting and constipation. She was about to be treated for peritoneal tuberculosis when these symptoms began.

The abdomen was distended asymmetrically and a very hard, fasciculate, painful immovable mass was felt on the right side. At operation an enormous pedunculated tumor of the left ovary was found. It had fallen toward the right side without torsion of the pedicle; the pedicle was bound by a triple ligature. The histological diagnosis was atypical seminoma with large cells. Radiotherapy was prescribed but was not carried out.

Ten years later the patient reported that her menstrual periods had begun at the age of 14 but had ceased 2 years later. Amenorrhea did not respond to hormonal therapy. An operation was performed which revealed the right ovary reduced to the size of a bean and the tube elongated and very slender. An infantile uterus was found on the left side, fixed between the vesical and the sacroiliac peritoneum. It was easily freed and at the last report the patient was in perfect health.

(The tumor here reported as a seminoma is the one which is commonly called a dysgerminoma, at least in the literature of this country, Germany and England. It is identical in its derivation and microscopic appearance with the seminoma of the testis. In the French literature the ovarian form of this tumor is still most frequently spoken of as seminoma, following the lead of Chevassu. It is often seen in young girls (carcinoma puellarum). As illustrated in this case, it is not infrequently encountered in patients showing some degree of sexual subnormality, as in pseudohermaphrodites. However, the majority of cases have occurred in patients with ostensibly normal sex development.—Ed.)

## FEMALE UROLOGY

### CARCINOMA OF THE FEMALE URETHRA (REVIEW OF THE LITERATURE AND REPORT OF THREE CASES)

S. G. CLAYTON

J. Obst. & Gynaec. Brit. Emp., 52: 508-12, 1945

Urethral carcinoma appears to be more common in the female than in the male, having been reported in 149 cases in males and in 262 cases in females. The true incidence is difficult to establish; it has been found, by one source, to account for 0.16 per cent of gynecological carcinoma, but was found only once in 43,000 gynecological cases by another writer.

Urethral carcinoma is usually a disease of postmenopausal women but it is seen in younger women. In the female the predisposing factors are less definite than in the male. The disease is seen mostly in parous women and most authors have mentioned trauma or chronic inflammatory processes as etiologic factors. Urethral caruncle is sometimes suspected to be a predisposing lesion, but the frequency of occurrence of caruncle makes it hard to be sure that the relation is not one of chance. The author finds no clinical or histological suggestion in the literature of any relation between caruncle and carcinoma.

The cases may be divided into 2 groups. One group represents urethral carcinoma, usually appearing as a malignant ulcer in the urethral floor and less commonly in the form of periurethral induration, extending for some length along the urethra. The 2nd group represents vulvo-urethral carcinoma which presents itself in 3 forms: (1) a vascular papillomatous nodule at the posterior margin of the urethral orifice; (2) a nodule that breaks down to an ulcer in the vestibule; and (3) a scirrhus induration around the urethral orifice. On microscopic examination the neoplasms are found to be of varying types. Squamous cell carcinoma, columnar cell carcinoma (both simple and adenocarcinoma), mucoid carcinoma and undifferentiated types all occur. In most series squamous cell carcinoma predominates. It is suggested that the well differentiated adenocarcinomata may arise from the paraurethral glands, but this is conjectural rather than proven. The squamous cell neoplasms appear to be radiosensitive; evidence is incomplete about the other types.

Urethral carcinoma produces little discomfort in the early stages and even after severe symptoms appear, patients often delay seeking advice so that extension to the bladder, vagina or lymph nodes may have occurred when the patient is seen. Perhaps the commonest early symptom is painful micturition. Bleeding is a common symptom, more especially with micturition. Local tenderness and dyspareunia occur with more superficial growths. Swelling of urethral or groin areas may be present when inguinal metastasis has occurred. The papillomatous vulvo-urethral type chiefly causes hemorrhage and pain, while the ulcerating type presents pain as the chief symptom. On examination the growth

may be seen projecting from the urethral orifice or felt per vaginam as a line of induration along the urethra. Enlarged inguinal glands are found in about 20 per cent of cases. Biopsy is the final and essential step in diagnosis, sometimes with the aid of urethroscopy.

In regard to treatment of the primary tumor, the choice between surgical excision and irradiation is obviously affected by the position and extent of the growth. If the posterior urethra is involved, excision results in incontinence unless suprapubic drainage or ureteric transplantation is employed. Irradiation has less operative risk although there is the possibility of both fistula-formation and stenosis. Radium needles can be inserted from above through the bladder as well as from below. It would seem reasonable to excise a small tumor complete at biopsy. In regard to the inguinal glands, there is the same choice between surgical excision and irradiation, there being fairly general agreement that surgery offers the best results.

The author presents 3 cases which are not of particular note except that the condition is a rare one.

(The rich and inaccessible lymphatic drainage of the urethral area makes carcinoma of this region as wicked as carcinoma of the vulva. Except in the comparatively rarely seen early stages, the surgical problem is a much more difficult one than with vulvar carcinoma because of the risks of incontinence unless the operation is combined with some such heroic procedure as transplantation of the ureters. In many cases, therefore, the gynecologist resorts rather unenthusiastically to radiotherapy, the ultimate results of which are usually disappointing, though there may be considerable temporary palliation and retardation. —Ed.)

## URINARY INCONTINENCE; WITH SPECIAL REFERENCE TO CERTAIN FACTORS WHICH ARE NECESSARY IN THE CURE OF THIS CONDITION

INGLIS F. FROST

Am. J. Surg., 71: 172-80, 1946

The author discusses the numerous operations which have been devised over a period of years for the cure of incontinence in the female. Some of these have given temporary relief, others permanent relief, but until there is a better understanding of the anatomy of the urethra and the mechanism of its control, all operative procedures will remain in the stage of experimental surgery.

While this paper is not an attempt to offer anything radically new in the way of an operation for incontinence in the female, it is an effort to evaluate important steps in the operation and to describe a new technic for the support of the urethra and bladder, especially where the incontinence has been accompanied by a urethrocele and cystocele. This technic is most clearly illustrated by figures 1 to 7, inclusive.

The important factors underlying successful cure in urinary incontinence are set forth. Free mobilization of the urethra and bladder is important in the cure

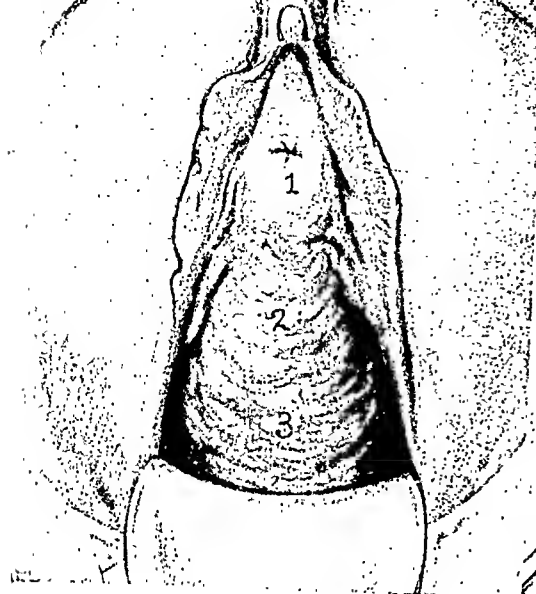


FIG. 1



FIG. 2

FIG. 1. 1, Urethra; 2, urethrocele; 3, cystocoele  
FIG. 2. 1, Mushroom catheter, size No. 12; 2, vesical neck of the bladder (note shortened urethra); 3, tip of mushroom catheter at site of urethrocele; 4, cystocoele—note thinned out portion of bladder wall; 5, smooth capsule of bladder wall; 6, anterior vaginal wall; 7, area of dissection under the pubic rami.

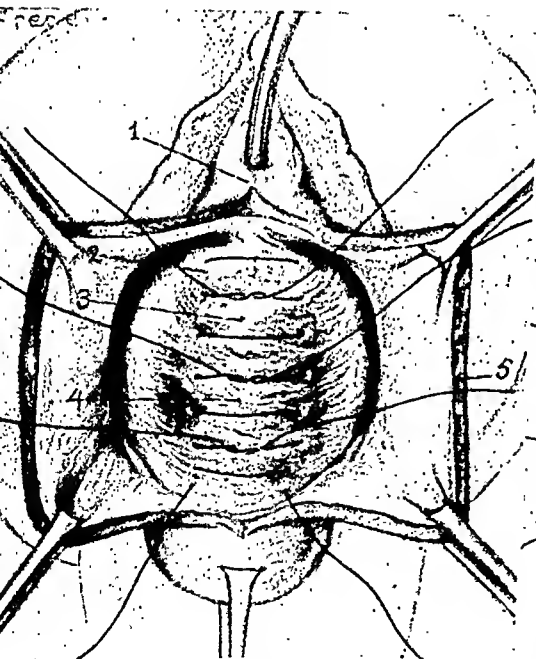


FIG. 3

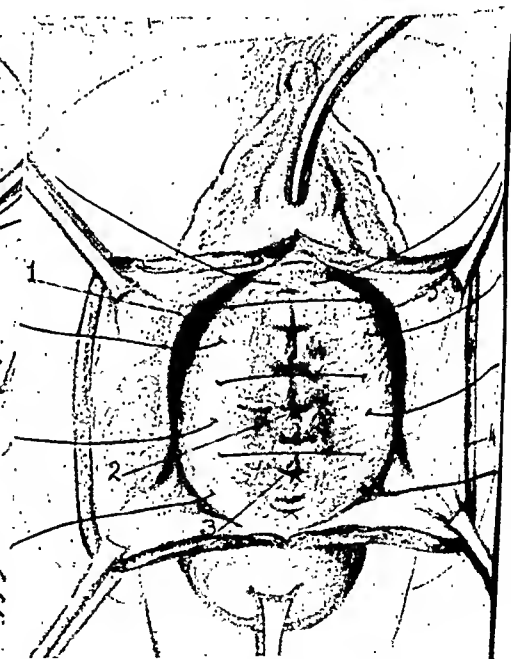


FIG. 4

FIG. 3. 1, Incision carried to within 1.5 cm. of external urethral meatus; 2, first suture placed high in the urethra; 3, second suture placed in region of the vesical neck; 4, remaining mattress sutures placed in region of cystocoele; 5, anterior vaginal wall.

FIG. 4. 1, Space under the pubic rami with free mobilization of the urethra; 2, first row of sutures tied; 3, second row of sutures in the bladder; 4, anterior vaginal wall; 5, smooth capsule of bladder wall.



FIG. 5

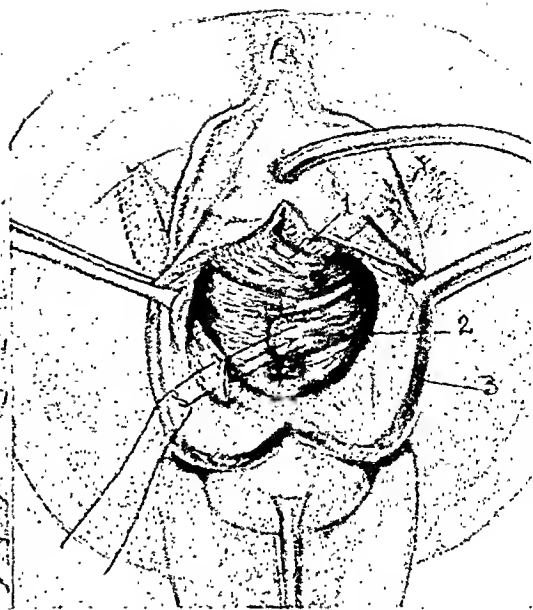


FIG. 6

FIG. 5. 1, Strip of tissue from the anterior vaginal wall (entire thickness); 2, second row of sutures in the bladder; 3, denuding the mucous membrane from the strip of the anterior vaginal wall.

FIG. 6. 1, Strip of tissue from the right side of the anterior vaginal wall sutured under the pubic rami of the left side; 2, excess portion of tissue sutured to that of the opposite side in the region of the vesical neck; 3, anterior vaginal wall.

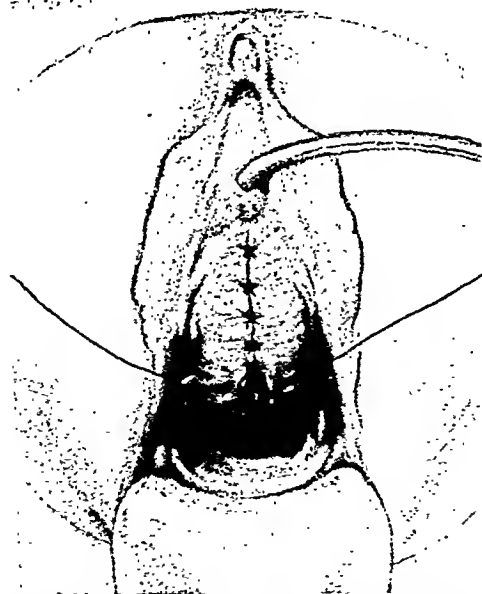


FIG. 7. Closure of anterior vaginal wall with interrupted sutures

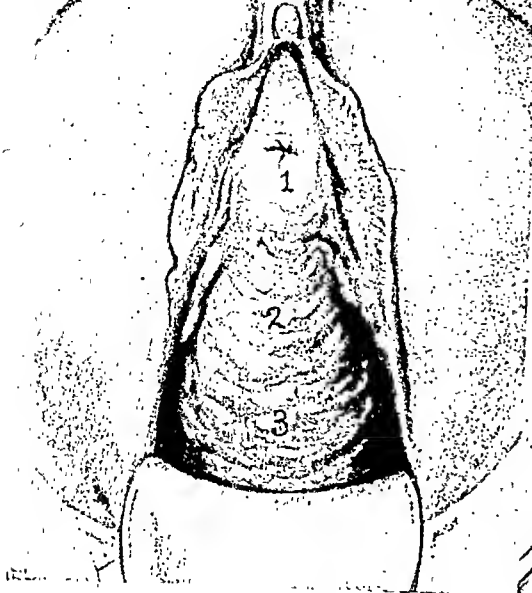


Fig. 1

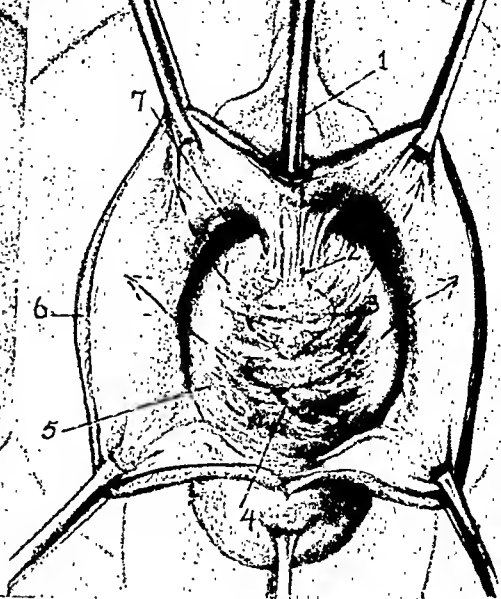


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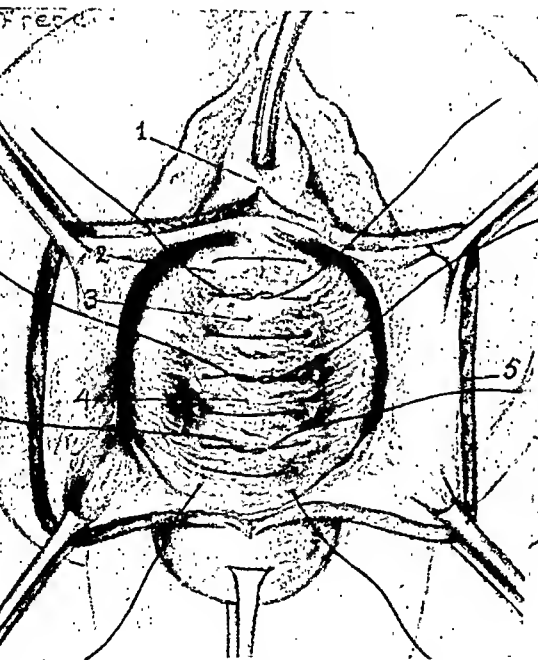


Fig. 3

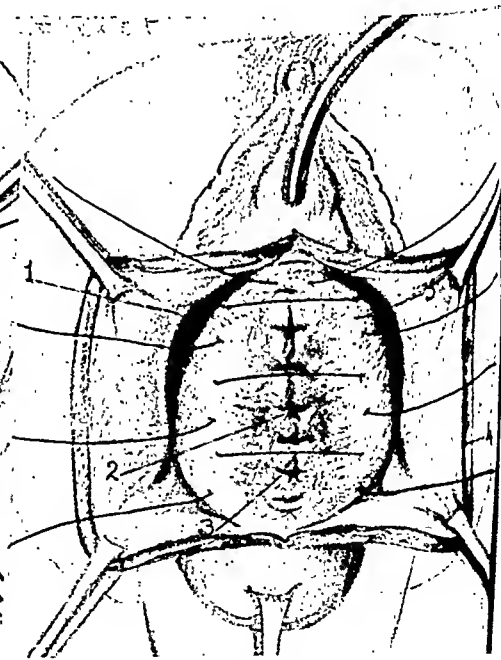


Fig. 4

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## OPERATIVE GYNECOLOGY

### THE SURGICAL CORRECTION OF CONGENITAL APLASIA OF THE VAGINA

N. F. MILLER, J. R. WILLSON AND J. COLLINS

*Am. J. Obst. & Gynec.*, 50: 735-47, 1945

Surgical correction of congenital absence of the vagina began only a little over a century ago, although the condition has been recognized since earliest antiquity. Today there is no reason why girls so afflicted should not benefit by modern surgical techniques and at an early age in order to minimize psychological trauma. The incidence of vaginal aplasia, although not definitely known, has been considered by Engstadt to be about one in 5000 births.

The condition represents an embryonal or developmental defect and may reveal itself as a partial or complete absence of the vagina. An important point to remember is that since the genital and urinary organs have a close embryonic origin, developmental anomalies of the urinary system may be associated with vaginal aplasia.

In 1904, Baldwin described a contemplated operation whereby he hoped to use a loop of terminal ileum or sigmoid colon, carrying it down through a newly dissected channel between the bladder and rectum. By 1910, he and others had successfully treated 6 cases in this manner without mortality. Schubert devised an operation wherein the rectum, except for the anal orifice and sphincter, was moved forward to form the vagina. The lower cut end of the sigmoid was attached to the anal orifice to retain continuity of the alimentary canal. Competition developed between the proponents of Baldwin's and Schubert's techniques, but the mortality and morbidity associated with both prevented an increase in their popularity and also served to stimulate the development of less hazardous forms of treatment. Frank and Geist devised one operation which called for dissection of a channel between bladder and rectum plus the lining of this channel with skin derived from the thigh.

The authors' interest in vaginal aplasia has been twofold: to discover the most satisfactory and simplest form of correction; and to study the behavior of the transplanted epithelium in those cases where a skin graft was used in lining the dissected channel. Their own experience has indicated that one of two surgical procedures is preferable. One is the formation of a channel between bladder and bowel and the continued use of an obturator until epithelization has taken place by ingrowth from the vestibular epithelium. The other method is dissection and the use of a split-thickness skin graft-covered obturator with subsequent take of the graft.

A brief outline is presented of the steps followed by the authors in the correction of their cases. Associated anomalies of the genito-urinary tract are carefully

of this condition. Plication of the urethra and the base of the bladder should be done without tension. Plication should include the urethra from a point just below and lateral to the external urinary meatus and should be continued posteriorly to a point which includes the vesical sphincter, thus lengthening the urethra and repairing the damaged voluntary muscle and relaxed vesical sphincter. Added support is given to the urethra and bladder by means of tissue strips excised from the anterior vaginal wall, and sutured to the undersurface of the symphysis and vesical neck, respectively.

Incontinence of urine in the female should be considered as the result of a damaged bladder and not as a separate entity. Its treatment should be directed toward restoring the urethra, vesical sphincter and the base of the bladder to their normal anatomical relationships. If these facts are kept in mind, we shall have gone far in arriving at a solution of this troublesome problem.

## NOTES ON THE TREATMENT OF VESICOVAGINAL FISTULA

W. R. MACKENZIE

J. Obst. & Gynaec. Brit. Emp., 52: 589-91, 1945

At least 3 months should have elapsed from the date of onset before operating upon the vesicovaginal fistula. Infection of the bladder should then be eliminated. To this end, the author employs a method of corking the fistula and washing out the bladder daily with sterile water. Also, by this means the vagina is kept dry and with daily douches soon regains a more normal condition.

Prolapse of the mucous membrane of the bladder into the fistula while it is being stitched may prevent the perfect coaptation of the muscular layer of the bladder. To prevent this, the author inserts a purse-string suture as near the refreshed edge of the fistula as possible, passes a sound through urethra and bladder and out at the fistula, and ties the free suture ends to the end of the sound. When the sound is withdrawn, the suture may be drawn to infold the edges of the fistula into the bladder.

Since in vaginal repair operations, the presence of even a small clot interferes with perfect union and since swabbing consumes time and is bound to injure the tissues, the author works entirely under a continuous irrigation of sterile water.

It is not necessary to subject the patient to the discomfort of self retaining catheters or to vaginal packing. A soft rubber catheter may be used every 4 hours for the first 48 hours and every 6 hours for the following 4 days. Then micturition normally will not harm the newly healed tissues. 5 figures.

(The procedure recommended by the author of inverting the prolapsed mucosa into the bladder is quite similar to that devised by Young and David for the repair of rectovaginal fistulas of small size. It should be helpful in the smaller fistulas, but would probably not be easily applicable to those of larger size with rigid surrounding tissues, as in these a purse string suture could scarcely be used.—Ed.)

## TUBAL STERILIZATION

RICHARD VAN DYCK KNIGHT

Am. J. Obst. &amp; Gynec., 51: 201-09, 1946

A series of 233 tubal sterilizations during a 10-year period has been reviewed by the author in an effort to determine which of the many tubal operations offers a simple, safe, sure and rapid method of permanently occluding the lumen of the tubes.

Since the first recorded attempt at tubal sterilization in 1880, many methods have been advocated and found not to be absolutely foolproof. In 1919, Madlener introduced a method in which a small knuckle of tube is crushed and a ligature of nonabsorbable suture material is placed across the devitalized area. In 1938, Von Graff reviewed the subject and collected 4279 Madlener sterilizations with 19 known failures. In 1930, Bishop and Nelms described a simple method which had been serving Pomeroy well for many years. In this technique, the tube is grasped at its mobile middle third, thus forming a loop. This, with a small portion of mesosalpinx, is ligated without preliminary crushing with fine absorbable catgut. The segment of tube above the ligature is then excised. A perusal of the literature indicates that this operation has not met with full recognition.

Of the 233 tubal sterilizations in this series, 174 or 75 per cent were Pomeroy resections with one failure. Other procedures used included 42 cornual resections, comprising 18 per cent, with no failures, and 14 or 7 per cent segmental resections with or without burial of stump, with one failure. All sterilizations were performed at the time of cesarean section, in conjunction with hysterotomy or as puerperal procedures.

During this 10-year period, the percentage of cesarean sections accompanied by tubal sterilizations was 16.6 per cent. Indications for sterilization at primary cesarean section were primarily medical.

In each of the 2 failures resulting in this entire series, the cause was faulty surgical technique. In the Pomeroy operation, it is important that a segment about  $1\frac{1}{2}$  to 2 inches be excised after ligation from the most mobile portion of the tube. The tiny fragments of tube, distal to the ligature following excision, become necrotic and absorbed. Just beneath the ligature each end of the tube becomes sealed off by peritoneum, inasmuch as the muscular wall slightly retracts. Following absorption of the ligature, the 2 ends of the tube retract for a distance of 2 to 3 inches; thus, the continuity of the tube is completely interrupted.

The author concludes that the Pomeroy sterilization is a safe, simple, sure and rapid procedure. The reported failures of this operation are 50 per cent fewer than for the Madlener sterilization. The Pomeroy sterilization avoids mechanical and biologic hazards to success, inherent in other types of tubal sterilization. 5 figures.

ruled out at the beginning. Customary preoperative preparation and general anesthesia are given. If a skin graft is to be employed, it is obtained at this time from the abdomen or thigh and the graft site is dressed. With the patient in the lithotomy position, a transverse incision is made in the vestibular mucosa about midway between the external urinary meatus and the posterior vaginal fourchette. The dissection is carried up the cervix, if present, or to the peritoneum. A pack is left in while the obturator is covered with the skin graft. This pack is removed and the graft-covered obturator inserted into the dissected channel where it is held in position by a perineal pad and T binder. An indwelling catheter is used until the 7th to 10th postoperative day when the obturator is gently removed. The newly formed epithelium-lined vaginal channel is inspected at this time and irrigated with warm saline. The obturator, cleaned and lubricated, is reinserted. It should be worn as long as necessary and be removed before defecating and before voiding. In patients with underdeveloped secondary sex characteristics, estrogen therapy may be helpful as a means of stimulating epithelial growth.

In order to compare the two procedures, the skin graft was omitted in 6 of the authors' series of 17 cases. Two of the 6 were unsatisfactory. Two of the remainder of cases wherein skin grafts were employed were unsatisfactory. The authors prefer the method of operation employing the skin graft unless it is contraindicated, as in cases where there is only partial absence of the vagina.

The authors observed the behavior of the epithelium in a new-formed vagina of one of their grafted patients one year after operation, throughout a complete menstrual cycle. The cycle of events was identical to that which occurs in the vagina of normal menstruating women. 11 figures.

(Norman Miller, from his own rich experience in the whole field of plastic surgery, is certainly well qualified to evaluate authoritatively the many procedures which have been devised from time to time to construct artificial vaginal canals. The earlier operations of the Baldwin and Schubert types were formidable procedures and associated with definite hazard. The results from the Baldwin operation, which I had occasion to perform in 5 patients, were excellent in every way, but there is no justification for operations of this magnitude at the present day, when we have available simpler and safer techniques which also give highly satisfactory results. Nor does there seem to be any reason for such difficult plastic procedures as the Frank-Geist tube-graft operation, calling for a high degree of plastic surgical skill with much chance for failure.

Like most gynecologists, Miller advocates the formation of a channel between bladder and rectum with the use of an obturator, but he feels that the additional use of skin grafts has given him the best results. Certainly even without the grafts the results are ordinarily very satisfactory, if I may judge from my own experience, which has been entirely with this technique. Miller and his associates also describe the acquisition of physiological cyclical changes in the mucosa of the new canal, confirming the two previous observations on this point by Whitacre and Wang (*Surg., Gyn. & Obst.*, 79: 192, 1944) and Ayre (*Am. J. Obst. & Gyn.*, 48: 690, 1944).—Ed.)

not prepared the vagina, provided the above-described technique is followed. 2 figures.

(It is difficult to follow the reasoning of the authors in pointedly avoiding any effort at vaginal sterilization before panhysterectomy, in spite of the fact that no peritoneal infections were encountered in their series. Certainly the vaginal canal cannot be completely sterilized, nor can the abdominal skin, nor the hands of the surgeon. And yet, if one has any faith at all in the principles of antisepsis, he will wish to approach the ideal as nearly as he can. My own practice and that, I believe, of most gynecologists, is to scrub the vaginal canal thoroughly with green soap and water, and then paint it heavily with one of the recognized disinfecting solutions. This does not mean that the abdominal procedure can then be carried out with complete disregard of the still present possibilities of infection from the vaginal canal. Most surgeons would still take every possible means of avoiding this, by measures quite similar to those which the authors describe. The combination of these with the preliminary vaginal preparation is the proper plan. Do them both. I remember hearing Dr. Charles Mayo tell the story of the man who got the following telegram from an undertaker in another city: Mother-in-law just died. Shall I bury her, embalm her or cremate her? He promptly wired back: Take no chances. Do all three.—Ed.)

## THE SUBPERITONEAL BALDY-WEBSTER UTERINE SUSPENSION

M. L. McCALL AND E. A. SCHUMANN

Am. J. Obst. & Gynec., 51: 125-29, 1946

The authors point out several weaknesses in the Baldy-Webster type of uterine suspension. The first disadvantage is the necessity of perforating the broad ligament in order to draw a loop of the round ligament through it. This has resulted in intestinal obstruction by the incarceration of a bowel knuckle into the opening in the broad ligament which had become enlarged by the traction of the uterus during several years. The 2nd disadvantage lies in the presence of the joined and uncovered loops of round ligament on the posterior surface of the uterus. This area offers a congenial site for the development of intestinal adhesions. Another disadvantage is in the possibility of failure of the suspension because of the lack of union between the serosa of the round ligament and the uterine serosa at the small area of suture contact between the two.

The subperitoneal approach is described which avoids the weaknesses of the old Baldy-Webster technique. In the subperitoneal approach, a vertical incision ( $\frac{3}{4}$  to 1 inch long) is made on the posterior uterine wall, its upper end corresponding to the intertubal line. This incision divides only the peritoneal covering of the uterus. With a slender pair of Mayo scissors, a subperitoneal tunnel is made in the posterior uterine wall, extending on either side to the insertion of the broad ligament. A slender, long-nosed curved hemostat is then introduced into the tunnels on either side, the anterior leaflet of the broad ligament is pierced, the round ligament is grasped at its most mobile point, and the loop of ligament is drawn back through the tunnel until it appears at the uterine

(This paper reviews very satisfactorily and fairly the various techniques of tubal sterilization, a number of the more popular methods being nicely illustrated with line drawings. The figures collected by the author appear to indicate a definitely lower incidence of failures after the Pomeroy procedure, as compared with the Madlener technique so widely employed.—Ed.)

## PANHYSTERECTOMY WITHOUT VAGINAL CLEANSING

T. CIANFRANI AND J. H. ZEIGERMAN

Am. J. Obst. & Gynec., 51: 109-13, 1946

Since the authors consider the vagina to be a septic focus, they believe it wiser to adopt measures of isolation of the said focus rather than trust to a necessarily imperfect sterilization of the vagina in the performance of abdominal panhysterectomies. A series of 130 cases of panhysterectomy is reported in this paper without preoperative sterilization of the vagina. There was no peritonitis or other complication which could be attributed to this technique.

No attempt whatsoever is made preoperatively to cleanse or sterilize the vagina. The following technique is applied during the operative procedure to isolate the infected vagina. Two sponges are placed in the cul-de-sac. A small incision is then made in the anterior fornix just above the palpated end of the cervix. An allis forceps is immediately placed on the cut anterior vaginal wall and the latter is held vertically in order to prevent it from coming in contact with the surrounding tissues and to prevent any drip. The vagina is then cut close around the cervix. An open sponge is then introduced into the vagina with long forceps. Additional Allis forceps are placed on the cut vagina anteriorly, laterally and posteriorly in order to maintain the vaginal cuff vertically and on stretch. The vagina is then closed and the sponges are removed from the cul-de-sac. All instruments are discarded. The operation is then resumed and completed.

A thorough study was made of the charts of the 130 cases operated upon in this manner. Fifty-three of the cases had appendectomies done and 27 had positive Wassermanns. The cases included in this report were generally of a very serious nature since most of the ward work is done on neglected cases. The complications encountered were: severe wound infections, 6; moderate wound infections, 3; indurated broad ligaments, 3; thrombophlebitis of the leg, 1; pyelitis, 1; and cystitis, 1. There were 2 deaths, both from pulmonary embolism. The results in this series approximate other studies of panhysterectomies *with* vaginal sterilization.

• Because they believe the use of soap and water and the application of antiseptics vaginally prior to or at the time of operation will not sterilize the vagina, the authors have emphasized the technique which prevents peritoneal contamination rather than sterilization of the vagina. A surgeon can therefore proceed with impunity in an unforeseen panhysterectomy, even though he has

result of the perineorrhaphy, 2 cases of hematoma with healing by second intention, 3 cases of vagino-perineal fistula and one of recto-perineal fistula.

In all of the 70 cases followed up, not a single recurrence had occurred. Some of them were observed during subsequent pregnancy with subsequent good results.

(An incidence of 3 cases of vagino-perineal fistula and one recto-perineal fistula among the 70 cases followed up seems rather high, since such sequelae are ordinarily readily avoidable by proper technique. Certainly it is advisable to amputate the cervix as a part of such operations in women beyond the reproductive age unless it is short and atrophic. In doubtful cases one may be inclined to leave it, but this is often regretted later, as it has an unhappy faculty of becoming elongated and pushing its snout down toward the orifice, so that the patient may find it difficult to believe that she is cured of her prolapse. Secondary amputation of the hypertrophied cervix is often necessary in such cases.

During the past few years an increasing number of South American visitors are being welcomed in our American clinics, and as a group they are most intelligent and appreciative, in addition to their traditional Latin charm and culture. I have been interested in the fact that they seem to love eponymic designations of operations even more than we Americans. Moreover, many of the proper names attached to operations by our good neighbors to the south mean very little to us Americans, since many of them have been imported from the European clinics. It is difficult to avoid eponymics in the designation of operations, but it is probable that the increasing intercommunication between North and South American clinicians will make it easier for us to understand one another in this as in other respects.—Ed.)

## PRESACRAL SYMPATHECTOMY FOR INTRACTABLE FUNCTIONAL UTERINE PAIN

EDWARD G. WATERS

Am. J. Obst. & Gynec., 51: 235-40, 1946

Of the various disturbances associated with menstruation, dysmenorrhea is patently the most common and most important of the functional disorders. The investigation of the cause of dysmenorrhea clearly involves a thorough gynecological examination as an initial procedure. Functional uterine pain commonly represents a psychosomatic disorder affixed to the predominant emblem of femininity. Psychotherapy offers more promise than correction of coexistent but completely innocuous findings of minor pelvic pathology.

When other treatment is inadequate, the pain may effectively be relieved by presacral sympathectomy. In patients with apparent emotional instability a preliminary low dorsal sympathetic block given at the onset of menstruation may be used as a diagnostic measure for pain-relief prognosis. Presacral sympathectomy will give the most notable results in cases with functional uterine pain similar to the cases quoted in this paper. It is also recommended as a surgical adjuvant where dysmenorrhea is an outstanding symptom-accompaniment to conditions such as impacted adherent retroversion and pelvic endometriosis with

incision. The loops from both sides are approximated with one or 2 sutures and the vertical incision in the uterine peritoneum is then meticulously closed with very fine catgut. Thus, the mechanical principles involved in the original Baldy-Webster technique have not been modified, but certain disadvantages have been corrected.

The authors discuss retrodisplacement of the uterus as to symptomatology, cause and treatment. 3 figures.

(Far be it from me to enter into any extended discussion of operations to correct retrodisplacements in the cases where operation is indicated, on such criteria as the authors indicate. It is probable that the most popular technique is still the modified Gilliam, especially the Simpson method. However, in many excellent clinics there is preference for the Baldy-Webster, the Ohlhausen, the Coffey or still other methods. As for the Lagerson-Schumann technique described in this paper, one who has never tried it might wonder if there would be any difficulty, or any annoying bleeding, in creating the long subperitoneal tunnels on the posterior surface of the uterus, where the peritoneum is so tightly fixed to the underlying muscularis.—Ed.)

## IMMEDIATE AND LATE RESULTS OF THE SURGICAL TREATMENT OF GENITAL PROLAPSE

MANUEL LUIS PEREZ, NORMANDO ARENAS E ISIDRO BOLLA

An. d. Inst. matern. y asist. social, Buenos Aires, 6: 9-19, 1944

From a total of 200 cases of genital prolapse operated on during the period of 1935-1943, 70 could be submitted to ulterior control, the results of which are reported in this paper.

As a rule, the Halban procedure was used in all degrees and varieties of prolapse observed in women within the sexual period of life, with the exception of 3 cases in which the Fothergill operation was done and 1 in which the Mayo technique was followed. In prolapses of old women, the Neugebauer-Le Fort colpocleisis was done in 8 cases and the Kahr operation in one.

When there was partial incontinence of urine associated with the cystocele, as a complement of the Halban operation the authors practiced the twisting of the urethra in 2 cases and its narrowing by Marion's technique in 5 cases, with satisfactory results. For repair of the cystocele, the authors followed Halban's procedure and whenever there was a retroversion of the uterus associated, the latter was fixed to the highest portion of the bladder peritoneum. Preference was given to low spinal anesthesia.

Amputation of the cervix was done whenever it exceeded 8 cm. in length; so was perineorrhaphy, with suture of the puborectal fibers of the levator, when there was a low rectocele or perineal laceration present.

Of all the cases operated on, only one death occurred as a result of pulmonary embolism. As complications, there was one case of bilateral phlebitis, and as a

result of the perineorrhaphy, 2 cases of hematoma with healing by second intention, 3 cases of vagino-perineal fistula and one of recto-perineal fistula.

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## PRESACRAL SYMPATHECTOMY FOR INTRACTABLE FUNCTIONAL UTERINE PAIN

EDWARD G. WATERS

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Of the various disturbances associated with menstruation, dysmenorrhea is patently the most common and most important of the functional disorders. The investigation of the cause of dysmenorrhea clearly involves a thorough gynecological examination as an initial procedure. Functional uterine pain commonly represents a psychosomatic disorder affixed to the predominant emblem of femininity. Psychotherapy offers more promise than correction of coexistent but completely innocuous findings of minor pelvic pathology.

When other treatment is inadequate, the pain may effectively be relieved by presacral sympathectomy. In patients with apparent emotional instability a preliminary low dorsal sympathetic block given at the onset of menstruation may be used as a diagnostic measure for pain-relief prognosis. Presacral sympathectomy will give the most notable results in cases with functional uterine pain similar to the cases quoted in this paper. It is also recommended as a surgical adjuvant where dysmenorrhea is an outstanding symptom-accompaniment to conditions such as impacted adherent retroversion and pelvic endometriosis with

probable adenomyosis uteri in young women. It should be strictly limited in its application to patients who first have been competently treated by nonoperative methods, and should be performed by surgeons capable of removing the plexus in its entirety. The pain tracts in the special visceral afferent fibers must be completely severed to effect complete relief.

The author describes 3 cases selected from a larger group because they illustrate in their case histories innocuous associated pathology, constitutional inadequacy, symptom transfer, and previous useless operations and hormone therapy.

The first case is that of a 19-year-old single patient with a history of an appendectomy and removal of 2 ovarian cysts 1½ years previously. Her complaint was severe dysmenorrhea since onset of flow, extremely severe for past 6 months and unrelieved by the past operation. Also she had had enuresis for years. Nothing was found in this patient except an innocuous lime-sized cyst of the right para-öphoron. The cyst was removed and a presacral sympathectomy was performed. The patient has had no pain with her periods since the operation. However, she believes her enuresis is worse; this may well be a symptom transfer. Psychoanalysis was recommended.

The second case is that of a married woman, 25 years of age, whose chief complaint was severe dysmenorrhea for 9 years, becoming progressively worse. Previous treatment included douches, dilatation and curettage, cervical dilatation, hormone therapy and all forms of empiric oral treatment. No pathology was found. Psychotherapy and hormone therapy brought no improvement. A presacral sympathectomy was carried out and except for one spell of pain with left sacroiliac strain and sciatica, the patient has since been well and free of all menstrual pain.

The third case is that of a 33-year-old woman, married and having a history of 2 dilatation and curettage operations and one cervical dilatation. Her complaint was severe dysmenorrhea since the start of menstruation, becoming worse in the past 2 years. This was unrelieved by any of the previous operations. Various medications and hormone therapy were ineffective. No pelvic pathology was found. A presacral sympathectomy was performed with complete relief of pain since operation.

(The author's discussion of functional pain appears rather ethereal, but the fact remains that presacral sympathectomy, involving excision of the sensory sympathetic nerve fibres of the uterus, is an accepted and often valuable procedure in otherwise intractable and severe cases of primary dysmenorrhea. However, it is an abdominal procedure, not altogether without hazard, not infallibly effective, and it needs to be done properly and thoroughly. It should certainly not be done unless non-surgical measures have failed to make the patient's lot at least tolerable, which means that no gynecologist should be able to report as large numbers of cases as have been reported by some. The operation serves a useful purpose when severe dysmenorrhea is found in association with such conditions as marked displacement or rather moderate endometriosis, in which it is often a matter of doubt as to whether such lesions can cause the severe dysmenorrhea of which the patient complains. The addition of presacral sympathectomy to any other indicated procedure in such cases will enhance the patient's chances for relief from her menstrual pain.—Ed.)

## STUDIES OF SURGICAL MORBIDITY. II. EFFECT OF PROSTIGMINE IN THE URINARY TRACT IN GYNECOLOGICAL SURGERY

H. O. JONES AND L. W. DOYLE

Am. J. Obst. & Gynec., 51: 184-91, 1946

Urinary tract infections are the most common complications following gynecological surgery. The purpose of this study is to compare the effect of prostigmine methylsulfate on the urinary tract of patients undergoing gynecological surgery with a similar group undergoing the same type of surgery who did not receive the drug. The effect of prostigmine methylsulfate on postoperative abdominal "gas pains" was also studied. Prostigmine methylsulfate may be described chemically as the dimethylcarbamic ester of 3-hydroxy-phenyl-trimethyl-ammonium methylsulfate. It is referred to hereafter in this study as prostigmine.

Of the 170 patients in this series, 75 received prostigmine and 75 did not. One ampule (1 cc. of the 1:2000) of prostigmine was given with the preoperative medication and one ampule was given immediately on return from surgery.

The incidence of postoperative urinary distress was the same in the treated as in the untreated group. The postoperative urinary laboratory findings were the same for both groups. The incidence of postoperative spontaneous voiding was the same in both groups.

"Gas pains" were somewhat lessened in the patients receiving prostigmine, but where obstruction existed, the discomfort was increased by prostigmine.

The amount of "residual urine" was found to be the same in the patients who voided spontaneously as in those who had to be catheterized for urinary distress or distention.

The authors conclude that prostigmine, as it was used in this study, was ineffective in preventing postoperative urinary infections.

## A CLINICAL STUDY OF EARLY POSTOPERATIVE AMBULATION IN GYNECOLOGY

PAUL F. STEINHART

Surg., Gynec. & Obst., 82: 348-55, 1946

The author reports 54 consecutive cases of gynecological operations; the first 17 cases were maintained on the conservative regimen of late ambulation and the following 37 cases in the group received early postoperative ambulation. It is concluded that early postoperative ambulation, *per se*, should in no way increase the incidence of wound disruption, postoperative incisional hernia, recurrent

cystoectoceles following plastic operation, or prolapse of the vaginal vault following vaginal hysterectomies.

In this series the temperature and pulse rates showed relatively little significant change due to early ambulation. Postoperative invalidism, both psychical and physical, was markedly reduced in those patients ambulated early. The nursing care requirements were markedly reduced.

No significant difference was noted in the requirements of postoperative catheterization in abdominal cases. In plastic operations and vaginal hysterectomies, however, an earlier return of bladder tonicity was suggestive in those patients ambulated early. Those patients ambulated early were relatively more able to move their bowels without the aid of an enema.

Sedation was rarely required after patients were ambulated early.

The average number of hospital days required by the patients ambulated early was 8.72 days and by those ambulated late 13.94 days, thus saving an average of 5.22 hospital days per patient for those ambulated early. The average convalescent period at home required by the patients ambulated early was 3.87 weeks and by those ambulated late 6.5 weeks. The average total convalescent period required by those who were ambulated early was 3.3 weeks less than that required by those ambulated late.

A study of the etiology and pathology of postoperative pneumonia, atelectasis, phlebothrombosis, embolism and infarcts indicates that early postoperative ambulation also offers advantages in prophylaxis.

Pain and discomfort as a result of early postoperative ambulation were not in evidence in this series. In fact, the patients who were ambulated early had less pain and discomfort than those who were ambulated late.

Early postoperative ambulation in plastic operations and vaginal hysterectomies should result in no greater incidence of recurrent cystoceles or prolapse of the vaginal vaults following vaginal hysterectomies. Anatomically, there is no evidence of added significant stress on the fascial and ligamentous supports from early ambulation.

A study of wound disruption and incisional hernia suggests that early postoperative ambulation should not in itself result in a greater incidence of wound disruption and incisional hernia providing, of course, the patient has received good preoperative care and the usual good operative technique. Follow-up in this series revealed no wound disruptions, no incisional hernias, no recurrent cystoectoceles and no prolapse of the vaginal vaults following vaginal hysterectomies.

The author concludes that early postoperative ambulation in gynecology reduces the usual postoperative invalidism, both psychically and physically, and results in a more rapid convalescence. Gastrointestinal and bladder tonicity may be increased. Very little, if any, sedation is required after early ambulation has been instituted. Nursing care is markedly reduced. There is an increased economy for the patient.

There is a definite advantage in early ambulation as prophylaxis against postoperative pneumonia, atelectasis, phlebothrombosis, embolism and infarcts.

(The policy of early postoperative ambulation has been urged from time to time for a great many years, but the present trend in that direction has gained far greater momentum than ever before. It has been encouraged by the necessity of rapid turnover in the overcrowded hospitals of today. I suppose that most surgeons are getting their patients up considerably earlier than formerly, and some have gone all-out along this line, allowing patients to get up the day after even very major operations. It is probably too early to make any worthwhile evaluations of the two general plans from the standpoint of the incidence of such postoperative complications as pulmonary embolism and incisional hernias, but this should be possible within a few years. I suspect that many patients will think it rather cruel to be forced to sit up a day or two after a big operation. Some years ago I underwent a cholecystectomy, and I can assure you that I had not the slightest desire to get up for the first few days afterward.—Ed.)

### THE EFFECT OF POSTOPERATIVE EXERCISES AND MASSAGE ON THE INCIDENCE OF PULMONARY EM- BOLISM AT CHELSEA HOSPITAL FOR WOMEN

J. P. ERSKINE AND I. C. SHIRES

J. Obst. & Gynaec. Brit. Emp., 52: 480-85, 1945

Postoperative exercises and massage were introduced at Chelsea Hospital for Women in 1937 in an attempt to reduce the incidence of pulmonary embolism. The incidence of fatal embolism following abdominal operations fell by more than 50 per cent in the subsequent 7-year period.

There were 2 deaths from pulmonary embolism following operations for the repair of prolapse in the 7-year period preceding 1937 and the same number in the subsequent 7-year period. Although postoperative exercises and massage have not reduced the number of fatal emboli following these operations, the authors have been impressed with the marked improvement of muscle tone and posture in these patients.

It was found that postoperative fatal embolism becomes progressively more common in the higher age groups; the average age of the patients was 50.5 years. The incidence of fatal embolism after subtotal hysterectomy was 0.449 per cent, after total hysterectomy, 0.401 per cent, and after Wertheim's hysterectomy, 1.46 per cent. There was one death from embolism in every 1088 non-abdominal operations. The embolisms following abdominal operations occurred as follows: 10 in the first week, 7 in the 2nd, 9 in the 3rd and one in the 4th week.

The chief aims of treatment with exercises and massage are as follows: (1) increased respiratory excursion resulting in improved venous return to the heart; (2) improvement of circulation and maintenance of muscle tone in the limbs; and (3) strengthening of abdominal and perineal muscles and later the development of correct posture. Some details of the exercises and massage employed are given.

(It is of interest to note that the incidence of postoperative pulmonary embolism following prolapse operations has not decreased since the institution of postoperative exercises in the group of patients studied by the authors. Others have reported definite decrease and the chief incentive for this plan of early postoperative activity has been the belief or the hope that there would be less hazard of this most distressing of postoperative complications. An increasing number of surgeons have adopted the plan of getting their patients out of bed very early after operation, but it is doubtful that this is the complete answer to the problem of pulmonary embolism.—Ed.)

## STERILITY

### OBSERVATIONS ON CERTAIN RHEOLOGICAL PROPERTIES OF HUMAN CERVICAL SECRETION

A. F. CLIFT

Proc. Roy. Soc. Med., 39: 1-9, 1945

Rheology is "the study of flow and deformation of matter". The object of this paper is to demonstrate 2 rheological properties of cervical secretion, namely, flow-elasticity and Spinnbarkeit (the capacity of liquids to be drawn into threads). The author also demonstrates the menstroscope, an instrument for the accurate objective measurement of flow-elasticity.

There is experimental evidence which suggests that the rheological properties of human servical mucus undergo a cyclic variation in the menstrual cycle, and bear direct relation to ovulation, to penetrability of cervical mucus by spermatozoa, and to pregnancy. At mid-cycle the secretion appears translucent and fluid; at other times of the cycle the samples appear more viscid; in pregnancy the mucus is characteristically thick, sticky and gelatinous.

Cervical mucus is not truly a viscous fluid and cannot be said to have a viscosity. Secretions such as cervical mucus are complex rheological systems and are characterized by properties such as: anomalous viscosity; elasticity; flow-elasticity; Spinnbarkeit; thixotropy; tack; stickiness; adhesiveness, etc. The changing viscosity of cervical mucus can be measured in a Scott Blair emptying-tube viscometer, but the apparatus is too delicate and complicated to be of practical everyday use as a test for ovulation or pregnancy.

Flow-elasticity and Spinnbarkeit, hitherto unrecognized rheological properties in human cervical secretion, both occur to a marked degree only in mid-cycle samples, and therefore form the basis for a rheological test for ovulation in woman. These properties are maximum only in "thin and translucent" samples, when penetrability and longevity of spermatozoa are greatest. These phenomena are absent in pregnancy samples.

The menstroscope is an instrument designed by G. W. Scott Blair for the measurement of flow-elasticity. When a material showing flow-elasticity is caused to flow along a tube, and the pressure is suddenly released, the material coils back toward its original position. The menstroscope consists essentially of a graduated glass capillary tube of about 0.75 mm. bore with the glass drawn down to 3 mm. bore. One end fits on to a 2 cc. Record syringe and a small side-tube 3 mm. bore is interposed between the tube and the syringe. With the side-tube closed, the cervical mucus is drawn into the capillary tube until the meniscus reaches the 7 cm. mark. The column of mucus is then slowly forced out of the capillary until the meniscus reaches the 4 cm. mark. At this point the side-tube is quickly opened, releasing the pressure on the mucus, the flow-elasticity of which

causes the meniscus to recoil along the capillary. The amount of recoil in mm. is noted. In performing the test, the following points should be strictly observed:

- (1) The cervix must be healthy.
- (2) Contamination with blood should be reduced to a minimum.
- (3) The specimen must be collected from the cervical canal.
- (4) Neither douching nor coitus must have taken place during the 24 hours preceding collection.
- (5) No antiseptics must be used in collecting the sample, only dry sterile instruments.
- (6) The elastic recoil test must be performed within 20 minutes of collection of the sample.

The test for Spinnbarkeit, the capacity of liquids to be drawn into threads, is carried out by drawing away a coverslip placed on a blob of mucus; the mucus is drawn into a long thread and the length of the thread which can be produced before rupture occurs is measured.

A rheological test for ovulation in woman is described, namely, the sample of cervical mucus is "runny"; homogeneously translucent; elastic recoil and Spinnbarkeit are maximum; tough bubbles which are difficult to break up readily form on homogenizing the sample; cellular content is minimal, and these few cells show movement typical of mid-cycle samples.

Considering the molecular construction of cervical mucus, it is suggested that the addition of donated cervical mucus (characterized by maximum elastic recoil and Spinnbarkeit) to semen, might be used with advantage in artificial insemination of cases of cervical hostility (absence of suitable cervical secretion).

Tack, a form of stickiness, is another independent property of cervical mucus but is only seen to a marked degree in pregnant samples. Tack is measured by quickly drawing a coverslip away from a blob of mucus placed on a glass slide. The whole surface of the blob adheres to the coverslip and can be drawn only a slight distance away from the slide.

A rheological test for pregnancy in woman is described, namely, the sample of mucus is thick; homogeneously opaque; the mucus is difficult to draw into the menstroscope; there is more or less absence of elastic recoil and Spinnbarkeit; tough bubbles do not form on homogenizing the sample; and tack is characteristically present. This description applies to samples as early as the 7th week of pregnancy.

It is believed that the described rheological phenomena and tests should prove of practical value in the recognition of ovulation and anovulatory cycles; in the investigation and treatment of cases of cervical hostility; as a useful tool in endocrinology of ovarian dysfunction; and as accessory tests for pregnancy.

## CYCLIC VARIATIONS IN THE VISCOSITY OF CERVICAL MUCUS AND ITS CORRELATION WITH AMOUNT OF SECRETION AND BASAL TEMPERATURE

ELLENMAE VIERGIVER AND W. T. POMMERENKE

Am. J. Obst. & Gynec., 51: 192-200, 1946

The authors made daily observations on 4 young healthy women, following one subject through 2 cycles and the other 3 through 4 cycles each. The quantity of cervical mucus present was determined by objective methods. These data were correlated with the basal body temperature curves and it was noted that the period of the cycle when the amount of mucus is greatest corresponds to the time of the temperature shift from a lower to a higher level, i.e., the presumptive time of ovulation.

On the basis of previous work, it would appear that the viscosity of the cervical mucus is an important factor in determining its penetrability by spermatozoa. No satisfactory method has been available for measuring this physical characteristic. The method presented by the authors in this paper has circumvented at least some of the difficulties encountered in the past and has proved useful in determining the cyclic variations in the viscosity of cervical mucus in normal women.

The material is collected by inserting an unlubricated speculum into the vagina to expose the cervix and then aspirating the cervical mucus into a weighed glass cannula. The amount is determined by difference, the total quantity present including mucus from the canal and the external os. Only that mucus obtained from the canal is used in the viscosity studies.

As used here, the term viscosity is defined as the time in seconds required to draw a column of mucus through a capillary tube a given distance at a given pressure as measured on a mercury manometer. In order to compare the daily determinations, all observations are corrected to conform with arbitrarily chosen standards. Duplicate observations are made whenever possible. The apparatus and exact procedure are illustrated and described.

In order to determine penetrability, a small amount of mucus is drawn into a capillary tube. A column of fresh semen is then drawn in, leaving a small bubble of air between mucus and semen. The capillary tube is placed on a slide and penetration of the sperm into the mucus is observed through the microscope. By using a stop watch and a calibrated mechanical stage, the rate of penetrability can be measured.

Results in this series showed that the viscosity is decreased during the period of increased secretion, both occurring at approximately mid-cycle. At this time a shift in the basal temperature occurs, this shift being useful in fixing the approximate time of ovulation. The penetration of cervical mucus by spermatozoa is correlated with viscosity. Maximum penetrability occurs when the viscosity is lowest.

The use of the methods outlined in this paper might give information concerning the likely time of conception and might prove helpful in the study of sterility.

(These observations are of great interest, and confirm those made in the obstetrical department of Johns Hopkins Hospital in 1940 by Lamar, Shettles and Delfs (*Amer. J. Physiol.*, 129: 234, 1940). For the present, it seems to me that their chief practical bearing would be in the interpretation of the viability of sperm recovered from the cervical canal in the well known Hühner test. They would suggest that the best time for the performance of this test would be at about the ovulation phase. Another article on this same general subject, by the same authors, appears in the January issue of the *Journal of Clinical Endocrinology* (6: 99, 1946). In the latter paper, the authors present evidence to indicate that the quantity of cervical mucus is more or less proportional to the amount of estrogen to which the patient is subjected, and that progesterone has no effect on the amount.—Ed.)

## BODY TEMPERATURE—A DIAGNOSTIC AID IN MENSTRUAL DISORDERS AND STERILITY

H. E. NIEBURGS

*J. Obst. & Gynaec. Brit. Emp.*, 52: 435-62, 1945

The author has investigated the vaginal and oral, or both temperatures taken simultaneously, in 41 women over 150 cycles. The 41 women included normal cases, postmenopausal patients, and patients suffering from various forms of primary and secondary amenorrhea, menorrhagia, intermenstrual bleeding and dysmenorrhea. The effects of estrogen, progestogen, androgen and vitamin B administration on the temperature curve were investigated.

Normal women exhibit a fall of temperature about one or 2 days before menses. During the menstrual period the temperature may reach a level as low as 97 degrees F. followed by a slight rise. The follicular phase is characterized by a low fluctuating temperature. Usually on the 14th day before the onset of the menses there is a sudden fall of temperature, perhaps as low as 97 degrees F., followed by a sudden rise. During the luteal phase there is a sustained elevation of temperature, reaching 100 degrees F. or higher, continuing until about one or 2 days before the menses. A slight decrease of temperature takes place in the mid-luteal phase, corresponding with the estrogenic peak. The author suggests that the decrease of temperature is an expression of estrogenic activity whereas the temperature rise is caused by the corpus luteum hormone.

In amenorrhea, oligomenorrhea, menorrhagia, dysmenorrhea and intermenstrual bleeding, the temperature curves are of great diagnostic value. The temperature in cases of secondary amenorrhea shows a persistently low curve, either fluctuating or constant. In oligomenorrhea the follicular phase is prolonged and menstruation occurs 14 or more days after ovulation. In menorrhagia there is constantly a prolonged follicular phase with delayed ovulation and short luteal phase. The temperature does not fall in the premenstrual phase but remains on a high level until the end of the menstrual phase. In dysmenorrhea

the temperature does not fall before the onset of menses but rises and does not decrease until the end of or after menstruation. Special significance is attributed to the changing relation of oral and vaginal temperature in dysmenorrhea. The oral increases at a greater rate than the vaginal so that it approaches or reaches the vaginal curve before or during menses. An exacerbation of pain was noted in those cycles in which approximation or union of the curves occurred. Patients with intermenstrual bleeding show a relatively high temperature curve with only minor fluctuations. The temperature during the menopause may be either high or low and shows a constant pattern or with very slight fluctuations.

In the therapy of menstrual disorders the temperature curve aids in deciding on the hormone and dosage to be administered, and indicates its degree of effectiveness.

The unmistakable sign of ovulation is of importance in cases of subfertility as well as for birth control owing to the easily recognizable safe and unsafe periods. No objections were encountered in this group of women to taking their vaginal or oral temperature, or both, for many cycles.

(It is to be doubted whether the temperature records in the various menstrual disorders studied by the author have as much practical significance as the author suggests. For example, it seems incredible that menorrhagia can show any sort of characteristic temperature curve, since its causation is so varied and since the endocrine mechanism in the functional group is so different in different cases. And the same thing applies to other menstrual disorders.—Ed.)

## CHARACTERISTICS AND VARIATIONS IN SEMEN SPECIMENS IN 100 NORMAL YOUNG MEN

JOHN MACLEOD AND LOUISE M. HEIM

J. Urol., 54: 474-82, 1945

In comparing the results obtained from the present study with those presented elsewhere, it is clear that the average semen quality of a group of young, unmarried men does not differ to any appreciable degree from that found in married men of known fertility. It also seems clear, as already indicated by Hotchkiss, that over an extended period in normal young men, the semen quality will not show any striking variation. There is no convincing evidence of seasonal variation in spermatogenesis.

In the present study, semen specimens were obtained at regular intervals over a period of years from 100 normal young men, most of whom were medical students, averaging 22 years of age.

The semen analyses from these 100 young men are compared with those presented in a study by Hotchkiss wherein most of the men were married and the average age was 31.5 years. The younger age group had a slightly higher average volume and higher spermatozoa counts, but the morphologic averages

were identical. It seems reasonable to assume that the spermatozoa count is likely to remain relatively constant over a period of years in the 20-40 year range, in spite of the sexual activity involved in marital relations.

In an attempt to substantiate the possibility of seasonal variations in temperature having some effect on semen characteristics, twice weekly specimens were studied for 11 months. Considerable fluctuations in sperm count were noted in individuals from week to week but the authors found no significant variation in the counts in relation to season. In one individual who acquired a severe cold with elevated temperature lasting for 2 weeks, the sperm count dropped from about 130 million/cc. to 28 million/cc. and the semen specimen did not regain its former quality for several weeks.

The authors were interested in determining after a period of sexual rest (7-10 days) the effect upon the quality of the semen specimen of ejaculation of 3 successive days. The answer is of obvious interest to the gynecologist, since in many cases the "fertile period" can be delimited to a period of 3 days. Of 18 individuals with good original specimens, only 2 showed enough decrease in count in the specimen of the 3rd day to warrant casting doubt of fertility on the specimen. Of 2 whose original specimens were only fair, the specimens on the 3rd day showed no serious depreciation in quality. Therefore, it is clear that if the original specimen is of good quality, 3 successive emissions at 24 hour intervals after a period of sexual rest will not result in a serious depreciation in the quality of the 3rd emission.

(Two important points emerge from this instructive study. First, the authors show that, contrary to the view held by a good many, the semen quality does not show any noteworthy variation over an extended period of observation in normal young men and that there is no evidence of seasonal variation, though it may show striking temporary deterioration with acute illness, if the one observation on this point may be considered in any way representative.

Even more interesting is the authors' conclusion that frequent coitus, for short periods at least, is not associated with decreased counts. Since frequent coitus during the wife's comparatively short optimum ovulation span is so commonly advised in the management of sterility problems, this observation is rather reassuring.—Ed.)

## THE VALUE OF PHYSIOLOGIC SUBSTRATES IN SPERM MIGRATION IN SELECTED CASES OF HUMAN INFERTILITY

SAMUEL L. SIEGLER

*Am. J. Obst. & Gynec.*, 51: 13-21, 1946

In this paper the author presents his experience with 2 of the problems pertinent to the process of human reproduction, namely: (1) a consideration of the fluid pathways in the female for sperm migration; and (2) their influence upon sperm motility.

Evidence is cited from the literature to indicate the importance of physiologic isotonic substrates to sperm metabolism and motility. It has been observed that maximum motility of human sperm suspended in Ringer-glucose solution is maintained for over 3 hours under anaerobic conditions but decreases markedly in the presence of air or pure oxygen. While sperm glycolysis remains relatively constant from specimen to specimen, large differences are found among individuals. The respiratory rate of spermatozoa varies inversely with the age of the specimen and directly with the number of cells per unit volume. Excess carbon dioxide produces complete immobility within a few minutes. Some have found that human sperm utilize glucose aerobically in Ringer-carbonate media, in human follicular fluid and in semen. The deprivation of sugar at 38 degrees C. causes failure of motility within 2 to 4 hours. Others have been able to report the revival of human and animal sperm after immersion in liquid nitrogen if they were later rapidly warmed to 35 degrees C. by plunging them into a suitable and balanced isotonic medium.

On the basis of these biochemical principles, 106 couples were selected carefully and Ringer-glucose isotonic solution was used precoitally as a vaginal irrigation. These couples gave a history of from one to 14 barren years and in all instances, the sperm studies, endocervical studies, tubal insufflation or hysterosalpingography, and endometrial biopsies had been made. During the relatively fertile period, as determined from the individual basal body temperature chart, the patient preceded intercourse with a vaginal irrigation, using this balanced isotonic substrate as the solution. Several cubic centimeters of the solution were retained in the vaginal canal. The author is able to report 29 successful conceptions, a salvage of 28.3 per cent, from this group of infertile patients. In 19 cases the Huhner test was found positive after use of the precoital sugar douche wherein previous Huhner tests, without the use of the glucose substrate, were found negative.

This procedure, because of its simplicity in application, is worthy of extended clinical trial and is recommended in those cases of infertility exhibiting no obstructive organic pathology.

(The period of viability of normal sperm, even in the vagina of the normal woman, is very short, and this fact does not seem of importance in lessening fertility. Whether the use of a precoital "physiologic substrate" of the type suggested by MacLeod and Hotchkiss in 1943 would enhance the patient's chances for pregnancy must still be considered uncertain, since experience with it has been so recent and so limited. While Siegler's results seem encouraging, I assume that in the cases in which he reports good results, this was not the sole measure employed for the relief of the sterility. When one looks back over the years and considers the various types of douches and irrigations that have been recommended for this indication, and recalls the sensational newspaper reports that a Vienna "professor" could influence sex determination by the character of vaginal douche given the patient, one can be forgiven for restraining one's enthusiasm for the clinical value of such adjuvants in sterility treatment as suggested by MacLeod and Hotchkiss, until more definite evidence is in hand. And this is said with full recognition of the high scientific standing of both these investigators.—Ed.)

LIPIODOL INTRAVASATION DURING UTEROSALPINGOGRAPHY  
WITH PULMONARY COMPLICATIONS

DAVID EISEN AND JACOB GOLDSTEIN

Radiology, 45: 603-07, 1945

One of the complications due to accidents in the course of uterosalpingography is intravasation of the iodized oil into the venous system of the uterus. Among the various factors likely to contribute to this accident are: (1) direct trauma to the endometrium by the uterine cannula; (2) excessive pressure during the course of injection; (3) recent operation on the uterus, particularly dilatation and curettage; and (4) injection too soon after a menstrual period.

The authors present the case of a 28 year old patient on whom lipiodol injection was done, employing the usual technic except that the amount injected was 15 cc. more than ordinarily used. Ordinary pressure was used but without manometric control. No difficulty was encountered. The film presented a bizarre picture. Not only was the uterus filled but its outer surface was visualized by contrast material within the venous plexus within and surrounding its walls. The uterine and ovarian veins and their tributaries were filled on both sides. The ovarian veins were completely filled, on the right side up to the vena cava and on the left up to and including the renal vein.

Later that day the patient developed a cough and elevated temperature of 102 degrees. Repeated pelvic films for several days showed decreasing amounts of lipiodol present. On the 9th day after uterosalpingography a chest roentgenogram was obtained which showed a dense, patchy opacity involving both lungs below the second ribs. The clinical condition of the patient was surprisingly good, out of all proportion to the appearance of the chest film. One month later the chest was re-examined and, aside from a slightly increased prominence of the peribronchial markings on the right side, the lungs were clear. The authors deduce that the unusual pulmonary densities in this case were attributable to residual phagocytosed lipiodol, perifocal pneumonitis about the emboli and actual infarction. 3 figures.

(The hazard of intravasation as a result of uterosalpingography is a real one, and reports of such cases are apparently increasing. One such report, that of Flew, was abstracted in the February issue (p. 149). A good review of the subject is that of M. A. Roblee and S. Moore, in the *South. M. J.*, 38: 89, (Feb.) 1945.—Ed.)

## MISCELLANEOUS

### PSYCHOSOMATIC ASPECTS OF GYNECOLOGY AND OBSTETRICS

GEORGE W. KOSMAK

New York State J. Med., 45: 2298-2304, 1945

The important role which the sexual characteristics of a woman play in her life suggests a close connection between the psychic and physical phases. Disturbances in either field can be handled more effectively if this fact is recognized and adequate attention given it by her attending physician. It is essential to investigate extensively her various complaints and not to ascribe them to purely psychic disturbances until a pathological basis can be ruled out.

The author discusses those topics in which it may be possible to develop a definite relationship between the somatic and psychic phases of a disturbance or illness. These are considered as follows: (1) menstrual disturbances; (2) pregnancy and certain associated conditions, such as hyperemesis, fear, etc.; and (3) the menopause.

Menstruation is a natural function, yet most girls begin without adequate knowledge as to its meaning. This brings up the problem of early sex education and the need for instruction, since the lack of proper knowledge is often productive of trouble later on. Among the complaints accompanying menstrual function is pain of varying degree. Experimental evidence has shown that there is little basis for the assumptions that such pain is attributable to a variety of anatomic causes. Operative procedures intended for relief are generally unsatisfactory and unnecessary. The pains are essentially uterine contractions initiated by the passage of accumulating blood and some women are naturally more sensitive than others. The therapeutic use of suppression of ovulation by estrogens, instrumental dilatation of a rigid cervical canal, cervical incisions and stem pessaries is questionable. The direct action of radium and x-rays on the ovaries, putting a temporary end to menstruation involves the risk of permanent amenorrhea and is an undesirable procedure. The resection of the presacral group of nerves, although good results are claimed, cannot be accepted without reservations.

After the exclusion of intrinsic organic factors, the patient should be assured that she has nothing to worry about in this connection and that simple remedial measures will be effective. This attitude should be supported by proper sedative measures; the milder barbiturates and some of the newer synthetic analgesics give good results, as do certain atropine derivatives. Heat and rest may be helpful. Most of these women are impressionable and must be made to believe that something can be done for them. The use of hypnosis has yielded favorable results but obviously must be carried out by an experienced practitioner.

Experimental evidence has been presented recently which showed that the

average pain threshold in 100 dysmenorrheic patients was lower than in equal control groups of nondysmenorrheics, postmenopausal women, and men. This evidence must be considered in the handling of these patients and places certain limitations on their psychiatric treatment.

The majority of women suffering from dysmenorrhea are otherwise well both mentally and physically and are quite contented if they can be relieved by sedative measures. The author advises attacking the situation by direct medical and other physical therapeutic measures before resorting to the more involved and time-consuming method of psychic analysis.

The author divides pregnancy abnormalities, as concerned with psychic disturbances, into 3 groups.

(a) *The Fear of Pregnancy*.—In order to evaluate the basis of this fear, one must consider both the real and the groundless causes. Fear of pregnancy may be very real in those women afflicted with previous crippling diseases, with former difficult labors, with families of small children or when the 3rd decade of life has been passed. With better knowledge of what can be done with adequate prenatal care and proper methods of delivery and aftertreatment, much of this uncertainty can be eliminated. It is important that a satisfactory relationship between the individual patient and doctor be established. There is statistical evidence that cardiac, nephritic, tubercular and other cases can be guided safely to a successful termination with skill and patience on the physician's part.

The fear of pregnancy is also sometimes associated with a distrust of the reliability of contraceptives which may result in a neurosis. The author feels that many cases of neurosis in women are dependent upon this factor and may be related directly to the production of certain pelvic disorders.

(b) *Hyperemesis*.—Successful management of "morning sickness" in a first often eliminates this symptom in subsequent pregnancies. Therefore, it is important to achieve success in treatment the first time. One must consider in each case the possible presence of a neurosis, a vitamin or food deficiency, an endocrine imbalance or some definite organic disturbance; one or all of these factors may be at fault. In severe cases of hyperemesis the resultant dehydration must be treated by rectal fluids and hypodermoclysis. A combination of psychic and medical therapy will accomplish results in many cases of ordinary or even aggravated pregnancy vomiting.

(c) *Sexual Frigidity, Dyspareunia*.—An underlying psychological factor as the cause of frigidity may be difficult to eliminate by the physician and since many women maintain a fairly happy existence without sexual satisfaction, it is an error to make such individuals feel inferior by too insistent efforts on the part of the physician to help them. However, when dyspareunia is present and can be traced to a definite pathologic cause, this should be eliminated. In a purely psychic case, a lack of response to psychotherapy may bring about a greater mental disturbance than previously existed.

The author suggests that, in referring to the menopause, the term "climacteric" be dropped from ordinary medical parlance, for it conveys the idea of a critical

period and thus magnifies a phenomenon fairly normal in most cases. The occurrence of a psychosis in connection with the menopause is without the province of the gynecologist and its handling should not be attempted through the medium of mere estrogen medication. The fear of cancer or pregnancy often develops and this calls for a more intimate cooperation between gynecologist and psychiatrist.

Psychotherapy, honestly employed, requires special training and often does not lie in the ability of the gynecologist to employ. He is accustomed to deal with anatomic abnormalities and his concepts of the nervous and emotional factors which may be involved have not been matured by previous education and training. The author feels that progress will not develop until the possible values of psychotherapy are more widely recognized and until its principles are more definitely presented and taught to medical students.

(No more timely subject for a presidential address before the American Gynecological Society could have been chosen than that of psychosomatics as applied to gynecology and obstetrics. It is of interest to note that in the same year the president of the other national organization, the American Association of Obstetricians and Gynecologists, Dr. Willard J. Cooke, chose a somewhat similar subject for his address. This is indeed the psychosomatic stage in medical practice. It represents an increasing recognition of the old dictum that a wise doctor treats the patient and not merely the disease.

The present paper abounds in good advice based on just this method of approaching problems of therapy in gynecology and obstetrics. For example, the author's attitude as to the treatment of dysmenorrhea is based on common sense and a probably disappointing experience with the countless waves of therapeutic fashion which have so ineffectively washed over this still unmoved rock of dysmenorrhea. Those who consider dysmenorrhea a purely endocrine problem and who place their dependence on endocrine therapy alone are just not good doctors. I myself employ endocrine therapy in only an occasional case. The younger generation of gynecologists especially will be benefitted by a reading of this paper.—Ed.)

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# *Obstetrics*

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## PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

### CARBOHYDRATE METABOLISM IN NORMAL PREGNANCY

DAVID HURWITZ AND DOROTHY JENSEN

New England J. Med., 234: 327-329, 1946

In view of the fact that true diabetes often begins during pregnancy and may be overlooked and the fact that pre-existing diabetes is often made worse by pregnancy, the authors have studied the effect of normal pregnancy on carbohydrate metabolism.

Serial glucose-tolerance tests were done on 25 normal pregnant women—at each trimester, immediately after delivery and several months post partum. The capillary blood-sugar level was determined fasting and  $\frac{1}{2}$  hour, one hour, 2 hours and 3 hours after the ingestion of 1 gm. of glucose per kilogram of body weight. At the same time urine sugar tests were made. All patients were kept on full normal diets to avoid the distorting effect of low-carbohydrate diets on glucose-tolerance curves.

The fasting blood-sugar levels during pregnancy were well within normal limits and over half were under 90 mg. per 100 cc. The post-partum group showed somewhat higher fasting blood sugars, only one patient having one under 90 mg. per 100 cc.

With rare exceptions, the peaks also were within normal limits. However, the 2-hour levels during pregnancy were abnormally high in 81 per cent of the cases. The highest percentage of abnormal 2-hour levels occurred in the second and third trimesters and after delivery, occasional values being as high as 164 mg. per 100 cc. The incidence of high 2-hour values persisted immediately after delivery but dropped sharply after the puerperium. All the 3-hour levels were normal throughout pregnancy and the post-partum period with one exception.

These data indicate that normal pregnancy exerts a deleterious effect on carbohydrate metabolism. It is during the second trimester that diabetes often appears and pre-existing diabetes is made worse. Obviously, a high 2-hour blood-sugar level cannot be considered diagnostic of diabetes during pregnancy, since it was present in 81 per cent of this series of normal pregnant patients. On the other hand, the 3-hour level was normal during pregnancy with one exception and may thus be used more properly as a criterion. Diabetes should not be diagnosed during pregnancy except by stringent criteria—a high fasting blood sugar (over 120 mg. per 100 cc., but preferably over 130 mg.) or a high 3-hour level (over 120 mg.).



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# *Obstetrics*

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In regard to the question of glycosuria during pregnancy, it is of interest that of the 4 patients who showed large amounts of sugar in the urine during the glucose-tolerance test, all but one had blood sugars over 180 mg. at the time of the glycosuria. Glycosuria during pregnancy usually is attributed to lowering of the renal threshold. Since, in these cases, significant glycosuria occurred in association with a marked elevation in blood sugar and thereafter dropped to normal, it is concluded that pregnancy glycosuria is probably due to a high alimentary hyperglycemia rather than to a lowering of the renal threshold. 2 figures.

(The statement of Hurwitz and Jensen that normal pregnancy exerts a deleterious effect on carbohydrate metabolism is in keeping with reports of other authors as reviewed in the February issue of the Survey, pages 8-9. But their finding that glycosuria in normal pregnancy is the result of alimentary glycosuria rather than a lowered renal threshold is at variance with most previous workers, many of whom have reported glycosuria with blood sugars of only 0.140 and 0.150 per cent and in some instances with maximal blood sugars of only 0.120 per cent. The present study, however, is a most careful one and Hurwitz' long interest and work in this field render the conclusions all the more authoritative. In view of these two explanations of pregnancy glycosuria now before us it is to be hoped that the above paper will stimulate further study of this important problem in other clinics.—Ed.)

## VITAMIN E DEFICIENCY IN THE MONKEY

K. E. MASON AND I. R. TELFORD

Anat. Rec., 94: 522, 1946

Four sexually immature monkeys, two males and two females, reared for 2 to 2½ years on a vitamin E deficient diet (500 gm. cooked rice of low germ content, 300 gm. skimmed milk powder, 180 gm. dry brewer's yeast, and 300 gm. of an E deficient diet used for rats), showed a progressive muscle weakness for several weeks prior to death or sacrifices. Histologically, the skeletal muscles showed considerable dystrophic change resembling that characterizing vitamin E deficiency in other animals. That a state of vitamin E deficiency had been induced was further supported by the presence of considerable amount of fuchsinophilous pigment in the smooth muscle cells of the walls in almost all organs of the digestive, respiratory and genitourinary tracts and, especially, in those forming the media of both arteries and veins throughout the tissues examined. Similar pigment was also abundant in connective tissue macrophages and cells of the reticuloendothelial system generally, and present in small amounts in certain epithelial cells (uterus, fallopian tube and kidney), but occurred only as traces in skeletal and cardiac muscle cells. Except for differences in pigmentation of muscle cells in certain locations, the histological picture closely resembled that observed after E deficiency in the rat and other laboratory animals. Four control monkeys of approximately the same age, reared on an adequate stock diet, showed no alterations of this type.

(It would be extremely interesting and of great practical importance to know how vitamin E deficient monkeys would behave in pregnancy. It will be recalled that in 1922 Evans and Burr showed that rats on a vitamin E deficient diet underwent estrus, ovulation and implantation satisfactorily but were unable to carry pregnancies to term because of retro-placental hematoma formation and fetal absorption about the 12th day. As a consequence this food essential came to be known as the "anti-sterility vitamin"; and on the basis of this rat work of Evans and Burr a huge superstructure was built, namely, the hypothesis that vitamin E deficiency is responsible for most ills that women are heir to, including sterility, abortion, premature labor, toxemia of pregnancy and particularly premature separation of the placenta. As every obstetrician knows, carloads of wheat germ oil have been sold for the treatment of these disorders.

Actually, the basis for vitamin E therapy in these conditions is rather weak. In the first place, nutritionists state that even the poorest human diets contain adequate vitamin E. Secondly, other species such as the rabbit do not respond to this deficiency by reproductive disturbances and there is no very good reason for believing that humans would do so. Thirdly, the few studies which have been carried out on vitamin E blood levels in normal and abnormal pregnancy do not indicate as yet that the complications mentioned above are associated with low blood levels of this vitamin. In our own laboratory we have now analyzed the sera of some 400 normal and abnormal pregnant women for vitamin E and feel certain that premature separation of the placenta and eclampsia are not caused by this deficiency and are very skeptical about its role in the other complications mentioned.—Ed.)

## PREGNANEDIOL EXCRETION AT THE ONSET OF LABOR

ROBERT LYON

*Am. J. Obst. & Gynec.*, 51: 403-410, 1946

It has been established that hormonal factors are responsible for the maintenance of pregnancy, the steroids undoubtedly playing a significant role. The salient steroid hormone during pregnancy is progesterone. Pregnanediol, the inactive alcohol isolated from the urine of pregnant women by Marrian in 1929, appears to be the end-product of a series of intermediate steps in the metabolism of progesterone. The purpose of this study is to measure the excretion of pregnanediol in the urine during the days immediately preceding labor, during labor and during the first few days of the puerperium.

The contention that labor occurs because of progesterone deficiency is supportable from observations on animals in which the ovaries are essential for the maintenance of pregnancy. Moreover, pregnancy has been prolonged by giving progesterone to rabbits just before term.

The author found that the onset of labor is preceded for several days by a marked decline in the excretion of urinary sodium pregnanediol glycuronide. The composite of 68 spontaneous delivery assays shows a steady decline from an output of about 30 mg. of sodium pregnanediol glycuronide 4 days before delivery took place to an average output of 19.5 mg. 48 hours preceding labor and 14.8 mg. one day prior to the onset of labor. The day of delivery shows an average excretion of 12.5 mg. On the first postpartum day the values dropped to 8.8 mg. and on the 2nd postpartum day to 4.6 mg. These declines are greater

than any previously recorded and the difference is attributed to the method and number of observations.

From the rapid decline of NaPG preceding normal labor, it is probable that very little progesterone is available at the onset of labor. It is implied that the concentration of progesterone available at the onset of labor is insufficient to maintain and continue pregnancy.

## THE CHANGES IN THE ELASTIC TISSUE OF THE UTERINE WALL DURING PREGNANCY AND AFTER PARTURITION

T. E. HUNT AND P. L. EVANS

Anat. Rec., 94: 472-473, 1946

Only a few fine networks of elastic fibers are present in the perimetrium and circular myometrium of nulliparous rats. Between the sixth and twelfth day of pregnancy these networks become more abundant especially in the circular myometrium. After the twelfth day, in implantation sites, the total amount of elastica may increase further, but due to rapid uterine expansion it appears rather to decrease. Just before parturition elastic fibers are stretched extremely thin and are difficult to see but do not disappear entirely. In the interimplantation sites where expansion is slight the increase is quite apparent and there is no relative decrease in the latter half of pregnancy.

After parturition the elastic tissue in the circular myometrium of former placental sites appears much more abundant than it did before pregnancy. It is somewhat increased in the perimetrium but the longitudinal layer remains practically devoid of elastic fibers. In the circular layer it is not distributed uniformly as stretched networks but rather as isolated, tangled and split threads arranged in spiremes of variable size. The tangling and clumping increases as the uterus reverts to its normal size and persists in some locations for at least 9 months. There is some indication, however, that the spireme arrangement of the elastic fibers gradually changes to or is replaced by new networks 4 or 5 months after parturition.

## MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

### CORRELATION OF PHYSICAL AND EMOTIONAL PHENOMENA OF NATURAL LABOR

GRANTLY DICK READ

J. Obst. & Gynaec. Brit. Emp., 53: 55-61, 1946

It is not generally recognized that in childbirth there is an "emotional labor" which is as definite and important as its physical counterpart. The present investigation has extended over a period of 15-20 years and observations have been made upon 600-700 cases which the author has attended personally, and other records of cases in which the mothers have been conscious at the birth of their children. Anesthesia, and little or no analgesia, was used in the 2nd stage of labor, although the women were offered it and knew it to be immediately available should they have discomfort which they considered unbearable or unjustifiable. It is suggested that the act of reproducing a species is unnatural:

(a) If it is an unbearably painful or alarming experience, and

(b) If drugs or anesthetics have masked the significance of either physical or emotional events.

Originally the author, from a scrutiny of cases, arrived at the hypothesis that—"Fear is in some way the chief pain-producing agent in otherwise normal labor." Today this is widely accepted as an established theory. In labor, fear produces tension in circular fibers of the uterus by stimulating the sympathetic nerve supply. Tension in these fibers opposes the action of the longitudinal muscle fibers supplied by the pelvic autonomic. Increased tension in the lower uterine segment and cervix causes pain, and pain intensifies fear. This Pain-Fear-Tension syndrome of labor may be controlled or avoided by correct interpretation of the stimulus.

Three important precepts should be kept in mind when considering childbirth as a natural phenomenon:

(1) Physiological labor exhibits certain emotional states. If and when emotional manifestations are abnormal, parturition becomes pathological and requires treatment by scientific means.

(2) "When a child is born there are 3 labors: (a) of the mother, physical; (b) of the mother, emotional; (c) of the attendant."

(3) "The art of physiological childbirth is the art of control," having 3 implications: (a) the woman's control of herself; (b) the obstetrician's control of the woman; (c) the obstetrician's self-control.

The phenomena of labor should be taught during pregnancy and recalled as the woman presents herself in labor. Such prenatal classes arouse enthusiasm and interest in childbirth and help establish a personal relation with the teacher

who may and should attend the woman during labor. When a woman's mind and body are in a happy, fearless condition there is usually a phase during the last 2 to 3 weeks of pregnancy when she becomes anxious for the birth of her child. If an attitude of fearless expectancy is carefully fostered, the early signs of the beginning of the first stage of labor are heralded with animation and exhilaration.

As the cervix dilates and uterine contractions become stronger, the woman becomes quieter. She realizes her helplessness but remains cheerful. From 2/5 to 3/5 dilatation of the cervix, her animation gives place to a more serious demeanor. She requires companionship, understanding and sympathetic encouragement. When the cervix is 3/5 dilated, the strengthening contractions not only invite conflict in her mind but are frequently coincident with physical tiredness. At this point soporifics are advised, not for pain, but for an hour or 2 of peaceful mental and physical relaxation which help maintain control and counteract the real test between 4/5 and full dilatation of the cervix.

The conduct of the transition from first to 2nd stage is the key to the success of the whole process. The woman needs kindly and firm sympathy; the induction of confidence is often of greater assistance to her than the early induction of anesthesia. The sacral region should be rubbed and she should be told that the pain in her back will diminish when the expulsive reflex is established. After full dilatation, with adequate instruction, she will hold her breath and gently bear down with the contractions. Her sensitiveness will decrease and she will relax between contractions. As the head descends, the onset of a dulling of her consciousness between contractions may be observed. She will become impatient, careless of her appearance and manner. When the presenting part reaches the pelvic floor, both woman and attendant may need to exhibit considerable patience. A feeling of mental and physical exhaustion will call for encouragement, explanation and confidence. Consciousness of the stretching vulva with the threat of increased discomfort may alarm her. At this point every woman should know that anesthesia or at least analgesia is within her grasp. The urge to escape is more frequently the result of fear than of pain. The woman should be warned of the rupturing of the membranes and the downward thrust and retreat of the head in order that she may not be frightened or disappointed by these things.

With the birth of the head there is gratifying relief. With the birth of the shoulders, the amnesic state disappears and she becomes alert. The author rotates the shoulders on delivery so that she may look down and see her baby. There is no thought of discomfort; the woman usually urges that the body be delivered to reveal the sex. Her physical appearance, mentality and behavior are completely changed and she becomes, in her happiness, a transfigured woman. She should be handed her baby as soon as the cord is divided. The influence of this state of physiological emotional ecstasy upon the uterus is immediate contraction. The 3rd stage of a happy mother is rarely longer than 20 minutes and blood loss is practically negligible. The author has observed that the placentae of girls bearing illegitimate babies are not infrequently retained.

This series of cases has demonstrated that suffering in physiological childbirth can be prevented by understanding and maintaining the controlled rectitude of the emotions, not for their elimination, but for their perfecting influence upon the physical phenomena of a physiological function. Certain benefits of this control include:

(1) The natural amnesic state of the 2nd stage produces the equivalent of complete anoci-association, excluding shock and postpartum neurosis.

(2) The desirable stage of transformation, which is obliterated by anesthesia, increases uterine contractions and expedites placental separation and expulsion.

(3) Interference is less frequently necessary.

(4) The uninjured birth canal, with appropriate exercises, rapidly regains its tone.

The mysteries of childbirth and the problems of reproduction will not be solved by innovations and interventions. From natural labors can be learned the significance of the physiological phenomena of parturition.

(Although most of us would probably not want to go all the way with Grantly Dick Read and relinquish analgesia and anesthesia in labor entirely, his works will well repay study by every practitioner of obstetrics. Indeed, no physician can read his "Revelation of Childbirth"—published in this country, I believe, under the title "Childbirth Without Fear", Harpers—without becoming a better, safer and more understanding obstetrician, nor without his patients assuming a happier and more wholesome attitude toward childbirth; and if I am not mistaken, moreover, they will have easier labors and want to have more of them.

Read's main theme in succinct form is that a tense woman means a tense cervix,—and what obstetrician of experience can gainsay that general observation? He reminds us that effective uterine contractions demand a nice co-ordination between the outer longitudinal muscle fibers of the uterus and the inner more or less circular muscle coat. When the former muscle layer contracts it produces a shortening of the organ and to some extent a compression about the fundus, both of which actions are designed to expel the uterine contents. This longitudinal muscle coat is innervated, according to authoritative anatomical opinion, by the pelvic nerve arising from the lumbosacral autonomic system. Now, the more or less circular oblique fibers of the inner layer are relatively sparse in the upper uterine segment, but increase both in size and number toward the cervix, in which disposition they differ from the longitudinal fibers which are more numerous and larger in the fundus and upper uterine segment, gradually decreasing in power through the lower uterine segment. These circular fibers form a distinct sphincter at the internal os. It is apparently their function to maintain the regularity of the form of the uterus but they also act as inhibitors to the expulsion of the uterine contents. As is well known, the external os in some cases appears to be almost closed at the onset of labor, whereas in others it is dilated to one or more finger-breadths. The dilatation of the cervix depends to a large extent upon the absence of tension in the circular muscle fibers of the lower uterine segment. These circular fibers, Read goes on, are innervated by the sympathetic nervous system.

From the above description—if correct—it must be clear that uterine contractions, to be effective, call for a correctly adjusted balance between the autonomic impulses to the longitudinal muscle coat and the sympathetic impulses to the circular muscle layer, and that any disturbance in either, whether in the direction of augmentation or diminution, will interfere with the normal course of parturition.

It is the core of Read's theory that *fear*, acting through the thalamus, which is believed to be responsible for emotional expression, brings the sympathetic nervous system into play and causes a tightening of the sphincter-like lower segment and that the resultant

tension; through ischemia, causes the pain of labor. The greatest difference, he believes, between normal visceral activity (emptying of the bladder and bowel) and uterine evacuation lies in the fact that labor is subjected to emotional influences, which by producing unnatural thalamic interpretation, subject the uterine musculature to efferent sympathetic responses which disrupt the neuro-muscular harmony of evacuation. The greatest of these emotional influences is fear, "the arch enemy of motherhood." If fear can be eliminated, Read insists, pain will cease. In support of this contention he points to a long series of cases over the past ten years in which means have been devised to eliminate fear and finds that, in varying degree, pain has been conspicuous by its absence.

Not a few neuro-physiologists may take issue with Read's explanation of the neuro-muscular physiology of uterine contraction on the grounds that it represents over-simplification and goes beyond the actual state of our knowledge at the present time; and some might even disagree altogether. However, Read cites an array of studies to support the above hypothesis including the work of Whitehouse and Featherstone (*J. Obst. & Gynaec. Brit. Emp.*, 30: 565, 1923; also *Brit. Med. J.*, 1923) and further investigation may very possibly demonstrate the general validity of this theory.

But even if the underlying basis for his contentions are not subject to proof at the present time, the clinical experience of a host of obstetricians will confirm his belief that fear and tension do make for difficult parturition. It is my own feeling that the wide-spread success of the barbiturates as analgesic agents in labor has been due in no small measure to their effect in allaying tension and in promoting relaxation. In this connection, it is instructive to note the behavior in labor of Oriental women, whose background, rearing and attitude toward childbirth are quite different from ours. It is the fondest hope of every Chinese girl to have children and many of them; and conversely, there exists no more abject and pitiful creature than the Chinese wife who is childless. Milleniums of a culture which has emphasized the family as its unit of civilization have placed childbearing on a pedestal and surrounded it with love and veneration,—the acme of happiness for every wife. As a consequence, Chinese women go through pregnancy with an exuberance and open pride quite rare in the Occident.

And how do these women behave in labor? This may best be described perhaps by saying that when I went to China a number of years ago, I was much interested in studying analgesia in labor because it was a subject much to the fore in American literature. But I quickly found, to my consternation, that these Chinese patients offered no material whatsoever for my proposed investigations because *they had virtually painless labors*; and looking back upon my experience there, which comprised several thousand labors in Chinese women, I can recall only two small groups of cases in which some form of pain-relief seemed called for: the patients with some mechanical obstruction to labor such as the osteomalacia group; and the hyper-sophisticated women of the upper classes, mostly graduates of American colleges, whose general background and attitudes were more Occidental than Chinese.

In strange contrast to these Chinese mothers was a group of Russian patients who also came under our care in childbirth. This was in the years following the Russian revolution and these pitiable Russian women, after experiencing unspeakable hardships in their escape from Red Russia, had somehow made their way across the frozen tundras of Siberia to Peking. Nervous wrecks, often without friends or relatives, they found themselves in a strange land amid alien tongues, confronting a pregnancy, which from the very nature of things was unwanted. I shall never forget the screams of these poor creatures in their interminably long labors. Our Chinese house-staff scarcely knew what to make of the picture. In the course of their experience with Chinese patients it just hadn't been brought home to them that labor could be so painful!

Like all pioneers, Read has met and will continue to meet much skepticism and even ridicule, but I am confident that he has a valuable message for every obstetrician, particularly in these busy days when assembly-line methods of practicing obstetrics have become all too common. Not just the above abstract or article should be read, but his book cited in the

first paragraph of this note. If obstetricians will but do so, I have a notion that many who come to scoff may remain to pray.—Ed.)

## EXPERIENCES WITH THE LABOR PROCEDURE OF GRANTLY DICK READ

BLACKWELL SAWYER

Am. J. Obst. & Gynec., 51: 852-858, 1946

The present paper is a report of 168 unselected, consecutive vaginal deliveries conducted by the method of Grantly Dick Read of London. These women were delivered in a small general hospital by the author personally, without the assistance of a resident.

The psychological processes in the female in preparation for her physiological functions are universally recognized. Read's theory is a deliberate attempt to harness, direct and control these feelings in a woman so that when she goes into labor, they may be turned into beneficial channels, and the woman is thus aided to have her baby.

The basis of the theory is that the pains of labor are caused by fear. At the beginning of labor, the cervix is pulled on by the muscle contractions from the fundus. The thalamus becomes aware of this through its connections with the sympathetic and autonomic systems, and an awareness of a new sensation is aroused. The thalamus informs the gray matter, usually by means of a misinterpreted impulse, that the woman is in pain. A reflex is set up through the sympathetic which overrides the relaxing efforts of the autonomic, causing not only an absence of relaxation but actually a spasm of the cervix. Thus real pain is produced which increases as labor proceeds.

The author outlines briefly the method of teaching a woman to have no fear, the art of relaxation and the nature of the process of labor. The technique is applied at the first prenatal visit. The result of such preparation throughout pregnancy is that labor becomes in the woman's mind a great and memorable occasion. Many of the women, whose records are discussed in this paper, speak of their labor as one of the happiest and most pleasant moments of their entire lives.

Of the 168 women delivered, 62 were primiparas and 106 were multiparas. Two multiparas with occipitoposterior positions and one multipara who had a face presentation suffered intensely and were not helped by relaxation. Of the rest, 12 multiparas were not helped and one refused to be bothered with it. The remaining 90 multiparas stated that they were greatly helped. They found the pain no greater than they were willing to bear and felt no need for other pain relief. Most of the women said that the method was marvelous and that they had actual discomfort only at the end of the second stage.

Two primiparas with deep transverse arrests required demerol, and rotation and forceps deliveries were carried out under anesthesia. Five others had very large fetal heads requiring low forceps. Two cases were breeches. Of the remaining 53 cases, the method appeared to succeed in 48. Ten of the 48 required small amounts of demerol to help them relax. In all primiparas a small episiotomy was done with the perineum infiltrated with novocain. The conduct of these patients was that of great calmness and cheerfulness. They stated that they enjoyed their labor because it was such a great event and the pains were not bothersome.

The author concludes that the method of Grantly Dick Read, when carefully applied, is valuable in relieving the pain of normal childbirth in about 9 out of 10 women. The method is a valuable contribution to obstetrics and deserves more research and application. The only drawback is that it is very time consuming. The study of the present series of patients and their labors seems to substantiate Read's view that any pain in excess of that which the woman is *willing* to bear is caused by fear.

## AN INVESTIGATION OF SOME OF THE CAUSES OF DELAY IN LABOUR

ELIZABETH A. NETTELL

Practitioner, 156: 203-205, 1946

It is the purpose of this paper to show that, in normal healthy women, uterine contractions during labor are directly affected by the attitude of the practitioner or midwife, and by the environment in which the patient finds herself.

A series of 75 cases has been classified into 7 groups of those delivered in various nursing homes, institutions and private houses. In this series there were 51 primiparae and 24 multiparae.

An analysis of the results in these various groups of patients shows that the length of labor depends to a large degree upon the state of mind of the patient. Patients who were disappointed because delivery must take place elsewhere than the place they had planned and in an atmosphere of rush and bustle were unable to relax between pains, became tired and uterine inertia followed. Women who appeared to have a definite fear of childbirth or to whom fear or nervousness was communicated by another person present at delivery had weak, infrequent contractions and long labors. Illegitimacy and a great deal of anxiety throughout pregnancy were also associated with delay in labor.

On the other hand, those women who were delivered in institutions where they were confident of good care or at home under the care of competent midwives had, as a whole, quick and normal labors. A cheerful, calm attitude in those persons attending the patients and a general atmosphere of friendliness and happiness appeared to be related to the occurrence of rapid easy labors.

## THE MEASUREMENT OF THE DIAMETERS OF THE PELVIC OUTLET

W. R. NICHOLSON AND R. TAUBER

Am. J. Obst. &amp; Gynec., 51: 538-543, 1946

The importance of a knowledge of the outlet measurements of the pelvis in the conduct of labor is illustrated by the fact that when the outlet is the area of contraction, dystocia may not be evident until labor is of many hours' duration, too late for cesarean section and too late except for a difficult forceps or even a destructive fetal operation.

The measurements of the outlet of the pelvis which should be taken routinely are: (1) the transverse diameter between the inner surfaces of the tubera ischii; (2) the anterior sagittal diameter; (3) the posterior sagittal diameter; and (4) the pubic angle formed by the junction of the rami of the pubis.

The authors' technique for the measurement of the postsagittal diameter is as follows: The instrument (which is illustrated in this paper) is placed between the most prominent points on the inner surfaces of the ischian tuberosities, said points having been marked with ink. This measurement having been obtained, the index finger is passed into the rectum, and without difficulty the little depression at the junction of the lower end of the sacrum and the first coccygeal vertebra is located. The hand is raised slightly until the rectal finger is bisected by the imaginary line between the ink marks on the tuberosities. The nail of the other hand marks this point and the pelvimeter gives the number of centimeters. To measure the anterior sagittal, the same method is used as for the postsagittal, namely, a finger in the rectum which easily reaches the junction of the pubic rami, then the imaginary line between the ink marks on the tuberosities is noted and a nail mark is made where said line bisects the finger in the rectum, the number of centimeters being shown by the pelvimeter. Having obtained this measurement, the estimation of the pubic angle, whether it is 90 degrees, or greater, or less, is simple. If the anterior sagittal is less than half the intertuberos diameter, the subpubic angle will be more than 90 degrees, while if the anterior sagittal be more than half the intertuberos diameter, the subpubic angle will be less than 90 degrees.

These measurements give a very definite picture of the capacity of the outlet and are of great value both in prognosis of labor and in the choice of treatment. 1 figure.

## UTERINE PAINS IN LABOUR

W. I. HAYES

M. J. Australia, 1: 196, 1946

The author names 2 criteria by which the normality of a labor may be judged: (1) the progress of the child, and (2) the pattern of uterine activity. Of the 2,

the latter is the more delicate, becomes evident earlier and is therefore the more important.

Except in the rare instance of true uterine inertia, the character of the contraction always reflects the progress of the child against the resistance offered to it by the pelvis and birth canal. Uterine contractions during labor vary in rhythm, duration, intensity and character, according to the stage of labor at which they occur. During the stage of shortening of the cervix the pains last 3 to 5 seconds, recur at regular intervals of 15 minutes to one hour and are usually felt solely in the abdomen. During the stage of cervical dilatation the pains last 20 to 25 seconds, recur every 3 to 5 minutes and, beginning in the back, pass around to the front. In the stage of descent or expulsion the contractions last 40 to 50 seconds, recur every 5 to 7 minutes, are typically "bearing down" in character and are assisted by voluntary contractions of the abdominal musculature. In every case the labor pains should be studied from time to time to see whether they conform to the normal pattern.

True uterine inertia is attended by infrequent, short, weak and ineffective contractions which are present throughout labor. Primary uterine inertia is due either to a reflex spasm of the circular muscle of the cervix or to lack of pressure by the presenting part on the internal os, as in disproportion, full bladder, placenta previa, etc. Secondary uterine inertia is initially due to obstruction of the child's progress. Hyperactivity of the uterine action, which is likely to lead to a state of impending uterine rupture, is also the result of obstruction, but in this case the child is attempting to pass through a partly dilated cervix, and this provides the stimulus which intensifies the forces of labor. For many years the mechanical factors of labor have been unduly stressed and it is hoped that in the future more attention will be paid to the physiological factors.

## THE PROGRESS OF LABOUR AND PALPATION

J. W. JOHNSTONE

M. J. Australia, 1: 196-197, 1946

Except in cases of gross cephalo-pelvic disproportion, it is not possible to predict the outcome of labor until the process is well established. The pelvis is moderately fixed but by no means circular. The all-important plane of the inlet is inclined at 55 degrees, with the forward-projecting promontory not much below the navel, so that the head passes down and back into the bed. The symphysis pubis is the outstanding landmark on palpation of the pelvic brim. The fetal head is compressible and ovoid in shape. The main art in obstetrics is to estimate the disposition of this ovoid body with respect to the sloping upper pelvic strait.

The author draws attention to that relationship between mother and fetus

described as the level of the presenting part, its degree of engagement, how far it has descended on the curve of Carus, or its relationship to the symphysis. When present in a primigravida at the onset of labor, floating head is a warning sign of possible disproportion, since lightening and fixity usually occur some weeks before.

Referring to palpation, the author states that the anterior shoulder is the only point sufficiently defined on the fetal body to be used as a landmark. When the head is completely above the brim the shoulder is 4 or 5 inches over the pubis, and when the head is fully engaged it is about 2 inches above the pubis. The fetal head, however, provides the main estimate of descent and disproportion and the methods used are the first and second pelvic grips and their modifications, which the author describes. The first pelvic grip of Pawlic can be used to determine fixity and to estimate overhang over the pubis. The second pelvic grip enables one to determine disproportion and overlap. Post-anal palpation during a contraction reveals that the end of labor is in sight if the firm resistance of the fetal head can be felt against the tissues behind the anus and in front of the coccyx.

By using these methods of external palpation, which can often be repeated and carry no risk, it is possible to determine the clinical progress of labor and, in most labors, to dispense with internal examination.

## THE MANAGEMENT OF LABOUR

R. M. ROME

M. J. Australia, 1: 199, 1946

The author stresses the importance of full instruction to the patient as to what to expect when labor begins and as to when she should proceed to the hospital. A primipara should go to the hospital when pains occur regularly at intervals of about 15 or 20 minutes. Multiparous patients should be admitted to the hospital if the membranes are ruptured, or at the first sign of abdominal discomfort associated with uterine contractions.

Several points are mentioned, concerning the delivery of the baby, which are useful if remembered by the practitioner. There is little chance of finding the chin until the anterior fontanelle is clear of the perineum. If difficulty is experienced, the Ritgen maneuver may be helpful. An attempt to deliver the head between pains is always associated with less damage to the soft parts of the mother. In delivering the anterior shoulder, it is often advantageous to apply pressure above the pubis in a caudal and backward direction. It is important that the mother be insured an adequate intake of food and fluid during labor to maintain strength, to forestall acidosis and to aid in the prevention of obstetric shock.

VINBARBITAL SODIUM FOR OBSTETRIC AMNESIA, ANALGESIA,  
AND ANESTHESIA

MILTON SMITH LEWIS

Am. J. Obst. &amp; Gynec., 51: 395-402, 1946

The results are presented of the administration of vinbarbital sodium to 622 patients for induction of amnesia, analgesia and anesthesia during labor. Of these, 469 received vinbarbital sodium orally in combination with scopolamine and, in addition, vinbarbital sodium intravenously for the completion of labor. The average dose was 9 grains orally and 10 grains intravenously. The remaining 153 patients received no other medication than vinbarbital sodium intravenously for induction of analgesia and anesthesia. The average dose was 15 grains.

Four hundred and fifty-nine (57.7 per cent) were primiparas and 263 (42.2 per cent) were multiparas. Spontaneous delivery occurred in 266 (42.5 per cent). Operative delivery occurred in 361 (57.5 per cent). Of the operative deliveries, 324 (89.7 per cent) were elective or outlet forceps, 30 (8.3 per cent) were breech extractions and 7 (1.9 per cent) were midforceps deliveries.

Of the 618 infants born alive, 530 (85.7 per cent) breathed and cried spontaneously. Seventy-two (11.6 per cent) were slightly asphyxiated but required no resuscitation. Fifteen (2.4 per cent) were moderately asphyxiated and required carbon dioxide and oxygen for resuscitation. The time elapsing between the administration of the drug and delivery or the size of the dose of vinbarbital sodium played insignificant roles in the incidence of asphyxia in this series.

The uncorrected fetal mortality was 3.3 per cent. Of the 19 infants that were lost, 9 died before the onset of labor and there were 6 nonviable infants. The corrected fetal mortality was 4, or 0.63 per cent.

Vinbarbital sodium appeared to have no effect on the duration of labor. Two hundred and fifty-five patients (40.9 per cent) were in labor less than 6 hours, 203 patients (32.6 per cent) from 6 to 12 hours, 140 patients (22.5 per cent) from 12 to 24 hours and 24 patients (3.8 per cent) from 24 to 48 hours. After the intravenous administration of vinbarbital sodium the uterine contractions were accelerated and dilatation progressed rapidly in the majority of cases. It was equally effective in both spontaneous and operative deliveries.

The "screaming" parturient who is nearing the end of her labor can be rapidly and effectively calmed with intravenous vinbarbital sodium. Slight to moderate degrees of restlessness occurred in 181 patients (29 per cent). Seventy-one patients who were slightly restless at the time of delivery were effectively controlled with local anesthesia. One hundred and ten patients who were restless during labor were promptly controlled by additional administration of vinbarbital sodium.

Complete amnesia was obtained in 61.6 per cent of all patients who received vinbarbital sodium orally with scopolamine. Complete amnesia was obtained

in 620 (99 per cent) following the intravenous administration of vinbarbital sodium.

No patients were encountered in whom this method of analgesia and anesthesia was contraindicated. No inhalation anesthesia was required in any instance. The incidence of postpartum hemorrhage was not increased. It occurred in 5 patients (0.8 per cent). There was no maternal mortality in the entire series. There was only one complication. This resulted from the accidental injection of vinbarbital sodium into the subcutaneous tissue.

The majority of patients slept soundly for from one to 8 hours following delivery. All expressed a desire for the same method of analgesia and anesthesia in their future deliveries. The results obtained in this series of 622 unselected private patients indicate that vinbarbital sodium is a most satisfactory agent for the induction of obstetric amnesia, analgesia and anesthesia.

## CAUDAL ANALGESIA WITH THE AID OF A NEW APPLIANCE; REPORT ON 250 CASES

MARK HORNSTEIN

West. J. Surg., 54: 56-58, 1946

The appliance, called the *Accouchaise*, is a couch assembly which, when mounted on a labor bed, supports the parturient in the prone position with the abdomen suspended through a central opening. It was designed on the basis of the observation that if a patient in active labor is placed in the knee-elbow position, the uterine contractions become more powerful, though less painful, and cervical dilatation is hastened. The author proposes the application of this device to the procedure of administering caudal analgesia. He has found that this appliance accelerates labor and, therefore, shortens the period requiring caudal analgesia, that it simplifies the technique of the procedure and that it enhances the safety of caudal analgesia.

With the patient resting prone on the appliance it is easier to locate the sacral hiatus and to enter the sacral canal because the overlying tissues are relaxed and the direction of the needle is straight rather than tilted sidewise as in the lateral posture. The flow of the solution is more even to the 2 sides and, when necessary, the patient can easily be tilted.

The safety of caudal analgesia is enhanced because it becomes a less protracted procedure with an accelerated labor and because the level reached by the solution can be controlled. This is because the sacrum slopes downward toward the waist while the spine slopes upward above the waistline when the patient is in position on the *Accouchaise*.

Caudal analgesia is started when there are strong uterine contractions at 5 minute intervals, if the cervix is thin and the patient in need of relief. A solution of metycaine, one and one-fourth per cent, is used. The results of the ad-

ministration of caudal analgesia to 250 private patients out of a total of 380 deliveries, with the use of the appliance described above, show that in 79.6 per cent, analgesia was complete and no other medication or anesthesia was employed. In 12.4 per cent there was total failure and in 8 per cent there was partial failure. No unfavorable sequelae were noted except backache persisting for a number of days, found mostly among the cases listed as failures. In 78 per cent of the cases only one to 3 hours were required and only one or 2 injections were given. There were 145 nulliparae in the series and in all but 5 of these analgesia was carried on for periods ranging between one and 4 hours.

## ANALGESIA IN LABOUR

W. M. LEMMON

M. J. Australia, 1: 197-198, 1946

The author discusses the relief of pain in labor with reference to the 6 basic methods found by Kotz and Kaufman to be in current use in American clinics. These are: (1) paraldehyde; (2) rectal use of an ether and oil mixture; (3) rectal administration of pentothal sodium; (4) morphine and scopolamine; (5) barbiturates; and (6) continuous caudal anesthesia. The danger of using morphine and scopolamine in multiparae is pointed out. This is because if the child should be born within 4 hours of the initial injection, the depression of the fetal respiratory center by the morphine may cause concern in the resuscitation of the child.

The author describes what he considers the most useful routine. Early in labor, chloral hydrate and potassium bromide, 30 grains of each, are given orally. When the cervix has been taken up and the os is beginning to dilate, hyosine compound A or B is given. Two hours later one two-hundredth of a grain of scopolamine is given and this dose is repeated every 2 hours or less often, according to the patient's requirements. The room is darkened and disturbance of the patient minimized.

The most generally useful of the barbiturates appears to be nembutal. It has been used alone and in combination with other drugs, notably scopolamine and paraldehyde. Lundgren and Bruce have found the combination of nembutal and scopolamine the most effective.

The most useful method for primiparae is outlined as follows: Early in labor chloral hydrate and potassium bromide, 30 grains of each, are given. When the cervix has been taken up and the os is beginning to dilate, 3 grains of nembutal are given, followed in  $\frac{1}{2}$  to  $\frac{3}{4}$  of an hour by  $\frac{1}{150}$  grain of scopolamine. For multiparae the nembutal dosage should be less, perhaps  $1\frac{1}{2}$  grains as an initial dose, followed in half an hour by another  $1\frac{1}{2}$  grains, if necessary.

Referring to continuous caudal anesthesia, the author states that although analgesia is perfect in the majority of cases, the risks are many. The main

danger is the injection of the solution into the subarachnoid space. Other dangers are infection and intravenous injection of the drug. The necessity for the constant attendance of a specially trained anesthetist proves yet another disadvantage. The author quotes Greenbill's suggestion that "continuous caudal anaesthesia will not become a part of our general obstetric armamentarium."

## ANAESTHESIA IN CHILDBIRTH

G. SIMPSON

M. J. Australia, 1—198-199, 1946

The ideal anesthetic agent and method of administration answering all requirements has not yet been found, but by various surgical anesthetics and other means, satisfactory relief can be given in all but exceptional cases.

The advantages and disadvantages of chloroform are set forth. The author believes that the falling off of the use of chloroform is a mistake, but its reintroduction would require careful training of those who are now accustomed to pouring on ether without fear of consequence.

At present ether is the most used anesthetic. It is considered safe and fool-proof, but although there is little risk of overdose, there are real dangers of post-anesthetic pulmonary complications. While nitrous oxide and air are suitable for analgesia and anesthesia in most normal cases, the concentration of nitrous oxide given does not allow deep anesthesia and is insufficient for forceps deliveries and in some cases of normal delivery. The advantages of this method are that it does not harm mother or baby and quickens labor. The author urges a greater use of gas.

No survey of anesthesia would be complete without reference to training in relaxation before confinement, which it is held allows painless childbirth, or hypnotism. There is thus a wide range of tried and tested anesthetics from which to choose. Whatever the method used, the aim is a healthy baby and an undamaged mother, and further, a mother whose comment would be "How marvelous it is to have a baby"—not, as is often heard, "Never again."

## MANAGEMENT OF THE THIRD STAGE OF LABOUR

W. D. SALTU

M. J. Australia, 1: 199-200, 1946

The sudden diminution in the size of the uterus following delivery predisposes to separation of the placenta from its attachment, and the oozing of blood from the placental site leads to the formation of the retroplacental clot. If the control

of the fundus is limited to light pressure, no harm is likely to result, but there is always the temptation to do more. Unnatural interference in the early third stage may be a menace to the formation of the retroplacental clot. Credé's original method of expressing the placenta with the first uterine contraction in 4 to 8 minutes was rightly condemned as being unphysiological. The author believes that expression by the Dublin method is advisable, usually within half an hour. In the majority of cases the third stage can be terminated in this manner after good contraction provided that some, if not all, of the signs of separation are present. Without the recognized signs of placental separation, and in the absence of undue hemorrhage, at the end of a half hour it is permissible to massage the fundus to see whether the placenta will separate. If not, at the end of an hour, Credé expression may be resorted to. If this is unsuccessful, one is probably dealing with a case of retained placenta.

After expulsion of the placenta one must be sure that the uterus is firm by suitable massage, but continuous massage on a uterus which is already firm does more harm than good. The routine administration of pituitrin and occasionally of ergometrine is considered wise.

## OXYTOMIC ACTION OF METHERGINE; A SYNTHETIC ERGONOVINE

E. W. CARTWRIGHT AND W. C. ROGERS

West. J. Surg., 54: 59-60, 1946

It has previously been found that Methergine, 0.2 mg., injected intravenously in parturient women at the time of the birth of the anterior shoulder of the baby, shortened the third stage of labor, reduced blood loss and produced no toxic or adverse collateral systemic effects. The detailed history and chemico-pharmacologic studies of Methergine have been comprehensively discussed by Kirchhof, et al. (West. J. Surg., 52: 197, 1944).

The authors administered the standard dosage of Methergine to 252 patients after the birth of the anterior shoulder, allowing one minute to elapse before the birth of the rest of the body. In several cases the drug was given during the placental stage of labor. An ergonovine preparation was given to 223 control patients. The results show that Methergine was as speedy in action, fully effective and equally as safe as the ergonovine preparations. The average time from the moment of administration until the birth of the placenta was 3.4 minutes for both the group given Methergine and the control group.

Less blood loss occurred with the use of Methergine than in the controls, probably due to the greater intensity and duration of effect of the synthetic drug. No toxic or adverse collateral systemic effects were observed.

## EPISIOTOMY AND PERINEAL REPAIR

G. BEARHAM

M. J. Australia, 1: 200-201, 1946

The woman's perineum and vagina should, after childbirth, be as near as possible anatomically to what it was immediately before conception. Consequently, the head should not be allowed to stretch the perineum for longer than an hour in a primigravida or half an hour in a multigravida. The author performs an episiotomy at the equivalent on the perineum of 5 or 7 o'clock; as a rule he carries the incision down to the muscle but not through the muscle.

The various types of lacerations found at the completion of the third stage of labor are discussed. If a laceration of the cervix is accompanied by severe bruising of the cervical tissue, unless hemorrhage occurs in this area, it is best not sutured but repaired some months later, as the bruised area generally sloughs. Tears involving the labia minora should be sutured with Number 2 plain gut interrupted sutures. Tears involving the posterior vaginal wall should be sutured with interrupted Number 2 chromicized gut sutures.

First degree tears of the perineum should be sutured as well as second and third degree tears. The torn tissues must be brought together accurately in layers, using Number 2 chromicized gut for interrupted sutures. In a third degree tear, the rectal mucosa should be sutured with interrupted sutures of Number 2 plain gut. The sphincter should be sutured with a figure-8 suture in 2 layers of Number 2 chromicized gut. In suturing an episiotomy incision, the author uses interrupted sutures with Number 2 chromicized gut. In the presence of a third degree tear, the bowels are confined for 6 days following repair.

# PATHOLOGY OF PREGNANCY

## THE TOXAEMIAS OF PREGNANCY

G. W. THEOBALD

J. Obst. & Gynaec. Brit. Emp., 53: 17-41, 1946

It is the purpose of this paper, in an effort to explain the eclamptic syndrome, to make certain observations on the mechanical factors which operate during pregnancy, to examine 2 of the "mechanisms" which have been suggested, (a) hyperfunction of the post-pituitary gland, and (b) placental infarcts, and lastly to evaluate the present position of the dietetic-deficiency hypothesis. This hypothesis postulates that the nutritional demands of the fetus on a mother suffering from multiple partial deficiencies, both of vitamins and essential minerals, deficiencies which usually antedate the pregnancy, are the underlying cause of the toxemias of pregnancy.

In Siam, with a population of some 11 millions, when antenatal clinics hardly existed and public health activities were in their infancy, eclampsia was all but unknown. In Ceylon, during the same period, the incidence of eclampsia almost certainly exceeded 28 per 1000 live births. In Hong Kong the incidence of the toxemias of pregnancy increased by over 100 per cent between the years 1939 and 1941, and was associated with an evident increase in the numbers suffering from malnutrition. The fact that eclampsia manifests a geographical incidence suffices to exclude from further consideration a number of the hypotheses which have been advanced to explain its etiology, since by universal consent no micro-organism is causally involved.

Any hypothesis should be considered against the following eclamptic postulates:

- (1) Its geographical incidence.
- (2) Hypertension.
- (3) Albuminuria.
- (4) Edema.
- (5) That one or all of these 3 signs (2, 3, 4) may appear independently of the others and that eclampsia may supervene in the absence of all of them.
- (6) The peculiar and almost pathognomonic lesions associated with eclampsia and conversely, that the liver of a patient dying from eclampsia may present a relatively normal appearance.
- (7) The higher incidence of the syndrome in association with primiparity and multiple pregnancy.
- (8) The incidence of eclampsia in association with hydatidiform mole.
- (9) That a woman may recover completely from an eclamptic attack and subsequently give birth to an apparently healthy child. Conversely, that eclampsia may occur many hours after an apparently normal delivery, and apart from any prodromal symptoms.

(10) That death of the fetus is frequently associated with an amelioration of the toxemic symptoms.

Concerning the operation of mechanical factors in pregnancy, the author has arrived at the following conclusions: (a) that the weight and size of the uterus may be a factor in the causation of albuminuria, edema and pyelitis, and (b) that the liver may, in certain circumstances, be seriously damaged by the eclamptic convulsions and possibly by the uterine contractions during labor. The simultaneously recorded rectal and intra-vesical pressures of a woman at term, while standing upright, correspond very closely, and exceed those similarly recorded in a non-pregnant woman by 11.5 mm. Hg. Both the rectal and intra-vesical pressures of a woman at term fall to below that of the atmosphere when she is placed in the Trendelenberg position. Therefore, it is evident that the difference in rectal pressure between pregnant and non-pregnant women is caused by the weight of the uterus. It may also be assumed that the bulk of the uterus during the last few weeks of pregnancy causes an elevation and relative fixation of the diaphragm, thus impeding the return of blood to the heart, increasing the general venous pressure, causing some measure of anoxemia, and predisposing the woman to albuminuria. The weight of the uterus and pressure of the fetal head might be expected to cause dilatation of the pelvis and calyces of the kidney, thus predisposing to pyelitis. The weight of the gravid uterus, when the woman is in the upright or sitting position, causes stagnation of the blood in the legs and consequent transference of water from the blood-plasma to the tissues. Primiparity, multiple pregnancy and hydramnios enhance the operation of all of these mechanical factors.

From certain of the author's experiments, it is reasonable to suppose that a liver, impaired either by imperfect nutrition or by some chemical agency, such as chloroform, may be seriously damaged by the mechanical factors associated with eclamptic convulsions and even by the "pains" of a normal labor. This possibility increases the difficulty of finding a safe anesthetic for use during delivery.

A clear distinction should be made between mechanisms which are thought to cause toxemic symptoms and hypotheses which purport to explain the genesis of eclampsia. Of these mechanisms, 2 have won the greatest support. The one attributes the toxemic manifestations to hyperactivity of the post-pituitary gland and the other to the toxic autolytic products which derive from recent infarcts in the placenta.

The author presents the following reasons to show that hyperactivity of the post-pituitary gland could not cause the manifestations of eclampsia and to suggest that post-pituitary extract does not contain a physiological pressor substance:

(1) Cushing's thesis that the hypertension and fits associated with eclampsia could be attributed to pituitary basophilism, associated with a basophilic adenoma of the pars distalis, no longer claims any general acceptance.

(2) Post-pituitary extract contains but 2 active principles, one which is oxytocic, and the other both pressor and antidiuretic. This extract causes an increased output of chlorides and stimulates intestinal peristalsis, whereas the

toxemias of pregnancy' are associated with a retention of chlorides and with coprastasis.

(3) Post-pituitary extract can cause proteinuria but tends to prevent edema formation.

(4) Post-pituitary extracts cannot pass through the membranes used by Anselmino, Hoffmann and Kennedy in experiments which demonstrated a pressor substance in the ultrafiltrates of blood from toxemic patients.

(5) If post-pituitary extract be added to normal blood, little of the activity can be recovered from the ultrafiltrate of the plasma; the extract seems to be largely absorbed to the red blood-corpuscles.

(6) From his own experiments, the author has not found evidence of a pressor substance in the blood of eclamptic patients.

(7) The author did find evidence of antidiuretic activity in the ultrafiltrates of blood from eclamptic and pre-eclamptic patients, but questions whether this may not have been caused by the almost inevitable toxic changes which occur in shed blood.

(8) It was found that the intravenous injection of that amount of post-pituitary antidiuretic substance which could effect a concentration of less than one in 4 milliards in the blood plasma exerts a measurable effect on water diuresis in a healthy man or woman. This raises the issue as to whether the post-pituitary substance can be regarded as a physiological pressor substance. The author suggests that the antidiuretic substance happens to be pressor when used in non-physiological amounts.

(9) The author found that amounts of infundin which inhibited water diuresis when injected intravenously, exerted little or no effect when injected intrathecally.

Although the autolytic products of the placenta are undoubtedly toxic, the available evidence suggests that the toxemias of pregnancy cannot as a rule be attributed to placental infarcts. It has been found that there was no significant increase in the incidence of infarcts in the placentas removed from toxemic patients. Furthermore, it is difficult to reconcile this hypothesis with the following clinical facts: (1) that a woman may recover from antepartum eclampsia and subsequently give birth to a living child; (2) that postpartum eclampsia may occur many hours after delivery; and (3) that neither placenta previa nor threatened miscarriage is commonly associated with toxemic symptoms.

If it is true that hypertension is as common in single as in married women who have borne children, and that a number of women who suffer from hypertension during pregnancy would have developed it whether or not they had become pregnant, then it clearly follows that such women should not be classified to any of the columns of the toxemias of pregnancy. It may well be that adequate nutrition might prevent the development not only of hypertension, but also of the cardio-vascular-renal sequence which ends in Bright's disease, but in the present state of our knowledge the confusion of "essential" hypertension with classical pre-eclampsia can but obfuscate the issue and impede the efforts to elucidate the cause of both conditions.

The dietetic deficiency hypothesis alone satisfies all the eclamptic postulates. The evidence in favor of this hypothesis may be summarized as follows:

(1) It is difficult to propound any explanation of the geographical incidence of the toxemias of pregnancy other than that which attributes them to malnutrition, seeing that by universal consent bacteriological agencies can be excluded.

(2) All animal experiments prove the necessity for an increased intake of certain minerals and vitamins during pregnancy.

(3) Necrosis of the liver may be caused in dogs by feeding them on a cooked lean meat diet and in rats by a diet deficient in protein.

(4) The mere addition of calcium to the diet of dogs can prevent death from carbon tetrachloride poisoning, while the intravenous injection of calcium gluconate can stop the convulsions, and prevent death from "milk fever," both in cows and in other domestic animals.

(5) It is believed by all authorities that multiple partial vitamin deficiency is common in England and throughout the world. Manifestations of vitamin and mineral deficiencies should therefore become evident during the course of pregnancy, and if the toxemias of pregnancy do not represent these manifestations then the mother invariably escapes at the expense of the fetus.

(6) This hypothesis alone can satisfy the eclamptic postulates, and it alone promises any hope of preventing the toxemias of pregnancy.

(7) It receives support from the success of antenatal clinics in preventing the actual onset of eclampsia.

This evidence, in favor of the dietary deficiency hypothesis, and in particular that afforded by the geographical distribution of the toxemias of pregnancy, appears to be very strong. Nevertheless, its proof awaits the satisfactory demonstration that they can be prevented.

Suggestions are made as to why the dietetic experiments so far made have signally failed to establish this hypothesis, the most important of which is that the "good" diet must be given before pregnancy begins.

The saving of maternal life which would result from the elimination of the toxemias of pregnancy would be great, but the consequent saving of fetal and neonatal life would be of immeasurably greater significance to mankind.

## ANTENATAL PEDIATRICS

LEONARD G. PARSONS

J. Obst. & Gynaec. Brit. Emp., 53: 1-16, 1946

This paper constitutes the sixth Blair-Bell Memorial Lecture, delivered before the Royal College of Obstetricians and Gynaecologists by the author who is Professor of Children's Diseases in the University of Birmingham. The paper deals with the influence of antenatal conditions on the fetus, stressing the importance

toxemias of pregnancy are associated with a retention of chlorides and with coprastasis.

(3) Post-pituitary extract can cause proteinuria but tends to prevent edema formation.

(4) Post-pituitary extracts cannot pass through the membranes used by Anselmino, Hoffmann and Kennedy in experiments which demonstrated a pressor substance in the ultrafiltrates of blood from toxic patients.

(5) If post-pituitary extract be added to normal blood, little of the activity can be recovered from the ultrafiltrate of the plasma; the extract seems to be largely absorbed to the red blood-corpuscles.

(6) From his own experiments, the author has not found evidence of a pressor substance in the blood of eclamptic patients.

(7) The author did find evidence of antidiuretic activity in the ultrafiltrates of blood from eclamptic and pre-eclamptic patients, but questions whether this may not have been caused by the almost inevitable toxic changes which occur in shed blood.

(8) It was found that the intravenous injection of that amount of post-pituitary antidiuretic substance which could effect a concentration of less than one in 4 milliards in the blood plasma exerts a measurable effect on water diuresis in a healthy man or woman. This raises the issue as to whether the post-pituitary substance can be regarded as a physiological pressor substance. The author suggests that the antidiuretic substance happens to be pressor when used in non-physiological amounts.

(9) The author found that amounts of infundin which inhibited water diuresis when injected intravenously, exerted little or no effect when injected intrathecally.

Although the autolytic products of the placenta are undoubtedly toxic, the available evidence suggests that the toxemias of pregnancy cannot as a rule be attributed to placental infarcts. It has been found that there was no significant increase in the incidence of infarcts in the placentas removed from toxic patients. Furthermore, it is difficult to reconcile this hypothesis with the following clinical facts: (1) that a woman may recover from antepartum eclampsia and subsequently give birth to a living child; (2) that postpartum eclampsia may occur many hours after delivery; and (3) that neither placenta previa nor threatened miscarriage is commonly associated with toxic symptoms.

If it is true that hypertension is as common in single as in married women who have borne children, and that a number of women who suffer from hypertension during pregnancy would have developed it whether or not they had become pregnant, then it clearly follows that such women should not be classified to any of the columns of the toxemias of pregnancy. It may well be that adequate nutrition might prevent the development not only of hypertension, but also of the cardio-vascular-renal sequence which ends in Bright's disease, but in the present state of our knowledge the confusion of "essential" hypertension with classical pre-eclampsia can but obfuscate the issue and impede the efforts to elucidate the cause of both conditions.

have a much more hopeful outlook. Various writers have expressed the views that therapeutic abortion should rarely, if ever, be resorted to in the pregnant patient with tuberculosis, and that the good or bad influence of pregnancy on tuberculous women is determined by whether they would have tolerated pregnancy well or poorly had they not been tuberculous. In 1940 Burke performed experiments on rabbits by injecting them with tubercle bacilli and allowing some to produce litters. X-ray and post-mortem findings in the pregnant rabbits compared with those in males and non-pregnant females revealed nothing to suggest that pregnancy had had an influence on the progress of the tuberculous infection. The results from studies by Steinbach and Klein suggest that the gonadotropic hormone may be a factor in the temporary amelioration of symptoms observed in tuberculous women during pregnancy. Other investigators have studied statistics in attempts to assess the influence of pregnancy on tuberculosis. Jameson, in an analysis of pregnant and non-pregnant tuberculous women, found no significant difference in the death-rate in the 2 groups. Hill, in a similar study, concluded that pregnancy had no appreciable bearing on the progress of tuberculosis.

Other authors believe pregnancy to have a harmful effect, but several of their papers are not convincing because of lack of complete and detailed information. Cutler considers that pregnancy has an unfavorable influence, but stresses the efficient protection afforded by adequate collapse therapy. He concludes that patients with advanced disease, or with active disease which does not respond to collapse therapy, do badly.

In concluding his review of the literature, the author presents the views of several writers who believe that abortion is rarely indicated in the tuberculous pregnant patient, and that adequate treatment of tuberculosis during pregnancy is important.

The present investigation embodies the results in a series of 177 consecutive unselected patients with pulmonary tuberculosis who have been confined in the Maternity Unit at Black Notley Hospital. Quiescent cases were admitted 4 to 6 weeks before confinement and active cases as soon as possible after the diagnosis of tuberculosis was made.

In the management of these cases, quiescent cases were encouraged to live an active sanatorium life while progressive cases were managed in accordance with the extent and activity of their pulmonary disease. Where necessary, active treatment such as collapse therapy was used. During labor, forceps were not applied routinely in the 2nd stage, but only when the indication existed; usually no woman was allowed to go more than 2 hours in the 2nd stage without their use being considered. Minnitt's gas and air apparatus was used in normal labors. It was found that artificial pneumothorax did not cause embarrassment to the mother in labor, and neither was it ever necessary to give a refill after labor to compensate for the alleged fall in intrapleural pressure, thought to occur as a result of the descent of the diaphragm.

Although true congenital tuberculosis is rare, post-natal infection is a real danger, and at Black Notley precautions include:

1. No mother or visitor is allowed to enter the nursery without permission.

one child. These findings substantiate the opinion that ectopic pregnancy is more frequent in the long-sterile or relatively sterile woman.

Past histories of the patients revealed that previous laparotomy, abortion and pelvic inflammation contribute to the incidence of ectopic pregnancy. A history of amenorrhea is considered a valuable diagnostic aid and was found to exist in 70 per cent of the patients.

The most outstanding symptom in these patients was lower abdominal pain which was present in all but one case (proved to be an unruptured interstitial pregnancy). In the majority of patients the pain was sharp in character and was referred to the affected side in 62 per cent of the cases. Fainting of varying severity was present in 35.4 per cent. Menstrual irregularity either following or without amenorrhea was present in all patients except 12, with dark chocolate-colored vaginal bleeding being noted at some time in 81.8 per cent. This type of vaginal discharge has become one of the more valuable symptoms which the authors use in diagnosis. Nausea and vomiting occurred in association with the pain in 30 per cent of the patients. Gastrointestinal symptoms and bladder symptoms were noted in a few patients.

Pallor was noticeable in 70 per cent of the group and abdominal tenderness was found in almost all. Pelvic findings showed a soft cervix in 35.4 per cent of the patients, enlarged uterus in 46.3 per cent, brownish vaginal discharge in 73.6 per cent and a palpable extrauterine mass in 93.6 per cent.

Transfusion was given to 57 per cent of the patients and proved to be a most important adjunct to surgical treatment. Surgical removal of the affected tube and the ovary on the same side was done in 67 per cent of the patients; in 30 per cent the ovary was left. It is imperative that both adnexal areas be examined at operation to exclude the possibility of bilateral ectopic.

It is the authors' opinion that surgical intervention should be limited to the treatment of the primary condition. Diagnostic curettage is of doubtful value. However, a "dry scrape" may be helpful. Diagnostic colpotomy was of limited application in this series and increased the postoperative morbidity.

There were 3 deaths in the series, presenting a mortality of 2.72 per cent. These deaths occurred on the 3rd, 5th and 12th postoperative days, 2 being from generalized peritonitis and the other from shock and peritonitis.

The authors describe 2 unusual cases. In the first, ectopic tubal pregnancy occurred following subtotal hysterectomy. The second was the occurrence of ectopic pregnancy in a tuberculous Fallopian tube. 3 figures.

## PULMONARY TUBERCULOSIS AND PREGNANCY

RAYMOND C. COHEN

Brit. J. Tuberc., 40: 10-48, 1946

In spite of the pessimistic attitude of the medical profession as a whole on the subject of tuberculosis and pregnancy, the majority of papers on the subject

measure to the effect of pregnancy, labor and the puerperium on pulmonary tuberculosis. Rather they would seem to be a measure of the natural processes of the disease, perhaps influenced by the associated changes produced by the care of the child in the woman's life. However, the author has been able to follow-up 120 patients, from 6 months to 2 years. Out of 87 quiescent, arrested or recovered cases followed up, 2 have died and 3 retrogressed. A total of 17 progressive cases are known to have died out of 58.

Follow-ups on 70 infants, 11 of whom were in contact with sputum positive mothers, showed that 4 of the 70 are known to have been infected with tuberculosis and 2 of these 4 have died. The mothers of 3 of these are known to have been infectious. Five other infants died from non-tuberculous conditions.

In the author's experience the worst cases have been those in whom tuberculosis was unrecognized or neglected during pregnancy. The value of routine chest x-rays in antenatal cases is suggested.

One of the arguments commonly employed by those who believe pregnancy to have a harmful effect on pulmonary tuberculosis is the sudden relaxation of support produced by the fall in the level of the diaphragm which is said to occur immediately after labor. The author presents reasons which contradict a belief that a beneficial effect is produced by compression of the lungs from below by the enlarging uterus and which show that a harmful effect produced by the emptying of the uterus is unlikely. Hence, the induction of pneumoperitoneum immediately after labor is a measure of no practical value.

It is accepted that a tuberculin-negative person exposed to infection has a slightly greater chance of developing the disease than a tuberculin-positive, but there does not appear to be any evidence other than hypothesis to indicate that changes in tuberculin allergy during pregnancy mean lessened resistance to tuberculosis.

It would seem reasonable to advise recently quiescent cases to avoid pregnancy for one or 2 years because of the strain imposed by the care of the infant. Patients treated by collapse therapy seem to have a slightly better prognosis than those in whom quiescence was secured by conservative measures.

When the pulmonary disease is quiescent or arrested and the woman is adequately supervised and placed under favorable conditions, therapeutic abortion is not justified.

(See editorial note after next abstract.—Ed.)

## PREGNANCY AND TUBERCULOSIS

DAVID A. COOPER

M. Clin. North America, 29: 1454-1462, 1945

The tuberculosis mortality curve in the 2 sexes runs parallel until the age of 15, when there is a sharp rise in the female mortality curve, with a high plateau, until the age of 35, when there is a rather abrupt drop, whereas in the male,

2. Every mother is shown her baby daily; if the mother is actually or potentially infectious she may not handle it, but the nurse shows it to her from the entrance to her cubicle. Both mother and nurse are masked.

3. Breast feeding is allowed only in recovered cases or possibly in quiescent cases of simple tuberculous pleurisy.

4. A mother must never approach her own or any other infant unless wearing a mask.

The present series of cases has been divided into 3 groups: (1) Arrested or recovered cases: those in which there has been no clinical or radiologic evidence of active disease for over 2 years; (2) Quiescent cases: those in which the disease, on all available evidence, showed no evidence of activity; and (3) Progressive cases: those in which there was clinical or radiological evidence of activity. The immediate results (within 3 months of labor) are shown in Table I.

TABLE I

CLASS OF CASE	NO. OF CASES	NO. SHOWING RETROGRESSION
Arrested and recovered.....	69	3
Quiescent.....	50	5
Progressive.....	58	15
Total.....	177	23 (13%)

Of the 3 arrested and recovered cases which retrogressed, 2 improved before discharge; of the 5 quiescent cases one improved; and of the 15 progressive cases 2 improved. Of the 15 progressive cases who retrogressed, 10 were suffering from advanced bilateral pulmonary tuberculosis in whom the prognosis would have been regarded as almost hopeless in the absence of pregnancy. Of the 23 cases in all groups who retrogressed, only 3 had difficult or complicated labors. On the other hand, 28 patients who had difficult or complicated labors did not suffer as a result. Of 58 cases with active disease on admission, 32 showed improvement after labor and 12 were quiescent by the time they were discharged. Of the 23 cases who retrogressed, 18 were primiparae and 5 were multiparae. Twelve were under 30 and 11 were over 30 years of age. In the entire series, of the 119 quiescent, arrested or recovered cases, 67 had been treated by collapse therapy and 3 (4.7 per cent) showed evidence of retrogression after labor. Fifty-two had been treated conservatively and 5 (9.6 per cent) of these retrogressed.

Except for a possible tendency to premature labor in cases with active disease, pulmonary tuberculosis appeared to have little effect on pregnancy and labor. On the basis of this study, it appears that tuberculous primiparae do not tolerate pregnancy as well as multiparae. The former have not had as many pregnancies to threaten their general health, but they are usually in an age group which has a worse prognosis, in regard to pulmonary tuberculosis, than that of the average multipara.

The late effects (after the first 3 months succeeding labor) are not a valid

(During the past century the pendulum has swung back and forth from conservatism to radicalism in the management of the tuberculous gravida, but over the last decade it seems to have settled, as attested by the above articles, on a conservative policy in most cases. Prior to 1850 pregnancy was thought to exert a beneficial effect on tuberculosis,—so much so that physicians were in the habit of advising marriage for tuberculous women in the hope that future pregnancies would benefit the disease. In 1850 Grisalles reported 27 cases and pointed out the deleterious effect of pregnancy on tuberculosis. Following this publication the management of these patients veered sharply to interruption, even in arrested cases, until 1906 when Rosthorn emphasized the fact that pregnancy may be relatively harmless in tuberculous women in whom the condition is quiescent and who have been without fever and hemoptysis for one year.

In 1929 Klemperer made an extensive review of the statistics bearing on the subject, particularly the very gratifying ones from sanatoria, and reported his own experience (*Zeit. f. Geburt. u. Gyn.*, 96: 1-16, 1929). On the basis of this survey, he reached the following conclusions, which represent in succinct form the policy which most obstetricians perhaps follow today: *Interruption of pregnancy on account of tuberculosis is never justified unless there is positive sputum or hemoptysis. If hemoptysis is persistent the pregnancy, if early, should be ended. In the presence of positive sputum, the course depends on the social and economic condition of the patient. If she is able to avail herself of institutional treatment, interference is not necessary.*

Certainly, a host of statistics from various tuberculosis sanatoria attest the fact that pulmonary tuberculosis is not affected by pregnancy *per se*. Thus, in one of the largest series reported, Marshall and his associates compared a group of 309 non-pregnant with 303 pregnant women in various stages of tuberculosis (*Brit. M. J.*, 1931, I, 140; *Lancet*, 1931, I, 186). In the group of "dormant" or "healed" cases, 2 per cent of the non-pregnant and 1 per cent of the pregnant cases died the first year. In the advanced stages of the disease 46 per cent of the non-pregnant women died, compared with 37 per cent of the pregnant group. Similarly, Forssner found no difference in the mortality of 341 pregnant women and 396 non-pregnant women who came to the out-patient department with tuberculosis. One of the most carefully studied series is that reported by Ornstein and Kovnat (*Am. Rev. Tuberculosis*, 31: 224, 1935). It comprised 85 pregnant women with tuberculosis, mostly advanced, observed at the Sea View Hospital, Staten Island, New York. The average duration of stay before confinement was 2.1 months and the average after delivery was 3 months. Of these 85 cases, 31, or 36 per cent, died; 15, or 18 per cent, were unimproved and progressed; and 39, or 46 per cent, improved. Therefore 54 per cent died or did poorly. Comparing these with a large group of women with tuberculosis uncomplicated by pregnancy at the Sea View Hospital, among 5470 cases, 1805, or 33 per cent, died; 1696, or 31 per cent, were unimproved and 1969, or 36 per cent, improved. In this group then, 64 per cent died or did poorly. Among the 85 pregnant women in the Sea View Series, 51 had a cavity formation. Of these 51, or 69 per cent, died within one year. This experience was almost identical with 700 caseous-pneumonia tuberculosis cases studied at the Metropolitan Hospital; in these the death rate was 68 per cent in the first year.

From a practical viewpoint it is important to recall that collapse therapy is frequently helpful in pregnant women as in non-pregnant, and that pregnancy is in no wise a contra-indication to this procedure. In a noteworthy clinical study of this question, Seeley, Siddall and Balzer reviewed in detail the results obtained in 54 tuberculous pregnant women who were given collapse therapy (*Am. J. Obst. & Gynec.*, 37: 741, 1939). Collapse therapy caused no serious ill effects regardless of the type and extent of the lesions; a majority even of their worst cases did well. Results were especially good when this type of treatment had been instituted before pregnancy or not later than the first trimester. Bilateral collapse was well tolerated in four very ill patients. However, although results for the series were generally good, there were at least 5 patients who would probably have fared better, in the opinion of the authors, if early therapeutic abortion had been done.

there is a gradual rise which continues well past this age. In Philadelphia, 20 per cent of deaths among women in the child-bearing age are due to tuberculosis. These statistics indicate that more than an accidental relationship exists between pregnancy and tuberculosis.

A high percentage of tuberculous women associate the onset of their tuberculosis with a pregnancy. The prenatal clinic is a better than average agent for tuberculosis case finding.

Two groups of factors associated with childbearing may influence the course of tuberculosis. First, experimental studies have shown that estrogen has a favorable influence and progesterone an unfavorable influence on resistance to tuberculosis in animals. Also it is clear that the presence of corpora lutea in the ovary is associated with an enhancement of the tuberculous process and acceleration of dissemination of the disease. If these hormones exercise similar effects in the human being, then it could be expected that in the first month of pregnancy, when the corpora lutea are more active, the disease would tend to spread. Second, pregnancy, in itself, induces physical and mental stress and strain and, if our present concept of the treatment of tuberculosis is correct, these additional factors of stress and strain predispose to the activation or reactivation of a latent or healed tuberculosis. Lack of rest, food and sleep may result from pregnancy and its complications and exert an unfavorable influence on tuberculosis. That the rising diaphragm, during the latter months of pregnancy, has a beneficial influence on the course of the tuberculosis is borne out by clinical experience, as is the claim that its sudden descent, following delivery, has a deleterious effect.

In view of these factors that might influence tuberculosis in the pregnant woman, it is surprising to find that adequately treated tuberculosis withstands pregnancy well. Ornstein and Cohn conclude that pregnancy has no effect on the course of pulmonary tuberculosis, and that the prognosis depends upon the character and control of the pulmonary tuberculosis, not upon the complicating pregnancy.

The importance of unrecognized tuberculosis should be stressed, as it is in this group that so many of the pathetic cases fall, in which a pregnancy is followed by a rapidly progressive and fatal tuberculosis. A roentgen examination of the chest of the pregnant woman is just as important as the routine Wassermann test.

The general trend is away from abortion. If the disease is recognized early in pregnancy, it is reasonable to put the patient on treatment and observe her from 4 to 6 weeks before a decision is reached. If the patient is past the third month of pregnancy when tuberculosis is discovered, interruption of pregnancy is rarely, if ever, justified.

Bed rest with adequate nutrition, supplemented by the various collapse procedures, such as pneumothorax, phrenic nerve interruption and thoracoplasty when indicated, forms the basis for the present day management of tuberculosis. From the standpoint of the phthisiologist, labor and delivery should be made as easy and short as possible by whichever method the obstetrician considers least shocking and in which there is the least amount of trauma to the patient.

and (4) Ulcerative lesions of the oral cavity and other mucous membranes, in most instances due to granulocytopenia.

In respect to the physiologic anemia of normal pregnancy, the authors believe that the changes in the peripheral blood noted in normal pregnancy are merely due to the hydremia, and possess no relation to an anemic state. The bone marrow, however, is stable, and the findings in normal pregnancy are constant. The finding of normoblastic bone marrow readily denotes the presence of a true anemia and determines the type of treatment needed. Megaloblastic anemia (pernicious anemia of pregnancy) can readily be diagnosed by the finding of a typical megaloblastic marrow. In cases of aplastic anemia the bone marrow reveals a marked hypoplasia of all the cellular elements. Sternal marrow biopsy is diagnostic and will rule out suspected purpura or agranulocytosis. In hemolytic anemia the bone marrow shows a normoblastic hyperplasia. Sternal marrow biopsy is only of a "negative" value in these anemias in that it rules out other types of blood disorders.

Acute and chronic infections of the head and neck are common causes of localized lymphadenopathy. Here sternal marrow biopsy will merely eliminate the possibility of a blood dyscrasia. Infectious mononucleosis may occur during pregnancy and in this event the bone marrow is hyperplastic with granulopoietic immaturity. The leucemias may usually be diagnosed from symptoms and peripheral blood findings and sternal marrow biopsy is merely confirmatory. However, in the subleukemic type, sternal aspiration is diagnostic if peripheral blood findings are obscure. Other disorders in this group in which sternal marrow biopsy may be helpful are Banti's disease, Hodgkin's disease and lymphosarcoma.

The sternal bone marrow findings in hemorrhagic disorders tend to denote the presence or rule out the existence of a true blood dyscrasia, and in true primary idiopathic thrombocytopenic purpura, offer a guide to treatment.

Ulcerative lesions of the oral cavity and other mucous membranes are found in a group of conditions called granulocytopenia. In these cases the bone marrow shows aplasia or a hyperplasia with a maturation arrest of the myeloid series.

Bone marrow biopsy is not the sole answer to hematologic diagnosis. The standard peripheral blood studies are still of major importance, and in many cases sternal marrow findings may be only confirmatory. Yet peripheral blood studies, especially in pregnancy because of the hydremia factor, often are inadequate or misleading. Sternal marrow biopsy then becomes mandatory. The characteristic marrow pattern noted in the various blood dyscrasias is of diagnostic, prognostic and therapeutic importance in the management of both the hematologic and obstetric problems. One of the greatest values of sternal marrow biopsy is its "negative value." The only exception is in cases of aleukemic lymphadenosis, when lymph node biopsy will be needed.

Sternal puncture with the concentration method of analysis is the preferred technique during pregnancy.

In a subsequent paper the same authors have reported observations on 34 pregnancies in 31 women subsequent to thoracoplasty (*Am. J. Obst. & Gynec.*, 39: 51, 1940). Their findings indicate in general that the majority of women go through pregnancy safely after thoracoplasty. In only 3 instances was mention made of dyspnea during pregnancy or labor but in one of these the dyspnea reached a serious degree during labor. One mother died and 5 others had serious exacerbations of the tuberculosis during pregnancy or within one year after delivery. It is noteworthy that thoracoplasty has been done successfully during pregnancy in at least 4 instances.

An important practical point brought out in the first Seeley paper cited above is that their tuberculous gravidæ who had neither collapse nor hospital treatment during pregnancy, suffered a very high mortality,—namely, 36.4 per cent, as contrasted with 11.1 per cent in the group subjected to collapse therapy and 10 per cent in their hospitalized non-collapse cases.

This brings us to the important role played by social and economic factors in the management of tuberculosis complicated by pregnancy. It may be true that pregnancy itself has little or no effect on tuberculosis, but the things which pregnancy normally brings with it, unless controlled, do exert a most deleterious effect. Chief of these is increased work, both before and after delivery, and everyone agrees that this is harmful to tuberculous women. If this additional work can be completely circumvented by prolonged hospitalization both prior and subsequent to birth, tuberculous gravidæ seem to do about as well as the non-pregnant. However, social and economic conditions sometimes make it virtually impossible to provide the institutional care which these women need; and hence, therapeutic abortion may still be desirable in some of these cases as indicated in Klemperer's dictum italicized above.—Ed.)

## BLOOD DISORDERS ASSOCIATED WITH PREGNANCY; THE VALUE OF STERNAL MARROW BIOPSY

J. R. WOLFF AND L. R. LIMARZI

*Am. J. Obst. & Gynec.*, 51: 447-466, 1946

In the past, the obstetrician's main interest in the blood findings associated with pregnancy has been in the clinical interpretation of the commonly noted lowered hemoglobin level and erythrocyte count seen in healthy individuals during pregnancy. In more recent years, the association of pregnancy and the various blood disorders has gained his attention, but unfortunately he has not made use of the sternal marrow findings. The hematologist, likewise, has not yet considered the problems of pregnancy in the light of the information obtained from bone marrow studies. It is only through cooperation of the hematologist and the obstetrician that such a relatively new procedure can reach its proper place in clinical investigation.

Clinically, all the blood disorders that may be associated with pregnancy can be classified in 4 general groups: (1) Anemia; (2) Conditions associated with enlargement of the lymph nodes, and splenomegaly; (3) Hemorrhagic disorders;

## SUBACUTE BACTERIAL ENDOCARDITIS COMPLICATED BY PREGNANCY, SUCCESSFULLY TREATED WITH PENICILLIN

CATHERINE DOBSON

Am. J. Obst. &amp; Gynec., 51: 427-428, 1946

In this paper the author reports the 16th case in a series of patients with subacute bacterial endocarditis treated with penicillin by Dr. Louis Katz at Michael Reese Hospital.

The patient, a 24 year old gravida ii, para 0, entered the hospital in January, 1945 at the 10th week of gestation for a therapeutic abortion, the indication being rheumatic heart disease present since the age of 8 years and complicated by congestive failure at 13 years. In May, 1943, a therapeutic abortion had been performed when the patient was 10 weeks pregnant and she had been advised against further pregnancies.

At the present admission the essential physical findings were suggestive of subacute bacterial endocarditis and blood for culture was obtained. The specimens revealed *Streptococcus viridans*. The abortion was, of course, contraindicated and the patient was referred to Dr. Katz for treatment. The penicillin sensitivity of the patient's organism was found to be good (0.01 unit per cc.) and it was felt that this indicated a good prognosis, judging by past experience with this type of organism. Penicillin was begun and 2½ days after the first injection the blood culture was negative.

At about the 16th week of pregnancy, the question was raised as to whether or not to interrupt pregnancy. The obstetric staff voted to allow the pregnancy to go on to term. However, after 5 weeks of penicillin treatment, Dr. Katz was not satisfied with the patient's progress. Although the blood cultures remained negative, she continued to have new petechiae and comparison of the response in this patient with others who had had a similarly sensitive strain of *Streptococcus viridans* was not favorable. This patient was pregnant; the others had not been, and it was felt that the pregnancy might be an unfavorable influence on the course of the disease. Accordingly, hysterectomy was performed and the patient made an uneventful recovery. Penicillin therapy was continued 2½ weeks postoperatively, completing 8 weeks of treatment.

On March 2, and on March 14, the sedimentation rate was found to be 12 and 11 mm. per hour, respectively. On admission the sedimentation rate had been 37 mm. per hour. How much credit for the normal sedimentation rate can be assigned to the removal of a possibly harmful pregnancy on the course of the septicemia is not clear because of the high sedimentation rates that normally occur in pregnancy. The patient was discharged on March 18, 1945, considered to have recovered from the subacute bacterial endocarditis. How much influence the pregnancy had on the course of the disease cannot be answered.

## INFECTIOUS MONONUCLEOSIS COMPLICATING PREGNANCY

E. HAROLD ENNIS

Am. J. Obst. &amp; Gynec., 51: 565-568, 1946

The patient, whose case report comprises this paper, presented herself for obstetric care in September, 1944. Her last menstrual period had been June 27, 1944. General examination was negative. The red blood cell count was 3,870,000 with 70 per cent hemoglobin and ferrous sulfate was prescribed. As pregnancy progressed the red blood cells and hemoglobin remained low, ranging from 3,000,000 to 3,600,000 and 56 to 63 per cent, respectively, in spite of continued large dosage of ferrous sulfate. In December the iron was discontinued because of marked gastric distress and the patient received no further iron for the remainder of pregnancy.

In January, 1945, she complained of marked listlessness and the red blood count was found to be 2,890,000 with 53 per cent hemoglobin. A transfusion of 500 cc. of titrated blood brought considerable improvement.

Lightening occurred in February and on March 10 she complained of marked malaise, anorrhexia and mental depression. Examination was negative except for a mild temperature elevation. Evening temperature elevation continued, with marked night sweats. On March 26, a differential smear revealed a rather marked change in the poly-lymph distribution, 54 and 40 per cent, respectively, so that infectious mononucleosis was suspected.

On March 28 labor was initiated by rupture of the membranes and a 4-pound, 13-ounce infant was delivered. On April 2 the white cell disproportion was even more marked and on April 9 the diagnosis was finally established by positive heterophile reaction in a dilution of 1:128. The subsequent course has been a general progressive improvement in the patient, as well as a gradual rearrangement of the white cells to the normal pattern.

Although the child's progress was normal, a surprising red count was found on May 1, 1945: red blood cells, 1,920,000 with 30 per cent hemoglobin. The parents were both RH-positive and the infant was RH-negative. The child was transfused with RH-negative blood, followed by immediate improvement in the blood count. However, in 4 days the count had dropped and iron therapy was instituted. Under this management the count remained at about 3,000,000 with 50 to 53 per cent hemoglobin. On June 16, the spleen became palpable. Since no progress was apparent with iron and liver extract, all medication was discontinued and, strangely enough, the red blood count rose to 3,860,000 with 60 per cent hemoglobin within 2 weeks, and splenic enlargement disappeared.

Whether or not mononucleosis in the mother was influential in the child's anemia remains to be proved.

## RUPTURE OF THE SPLEEN AS A COMPLICATION OF PREGNANCY

ELIZABETH CONFORTH AND JOHN CARANGELO

Am. J. Obst. &amp; Gynec., 51: 429-431, 1946

A case is reported of thrombosis of the splenic vessels with rupture of the spleen occurring during late pregnancy. Only 22 other cases of splenic rupture occurring as a complication of pregnancy have been recorded.

The patient, a 30 year old Negro woman, was admitted to the hospital in her 36th week of pregnancy complaining of severe frontal headache. For the past 2 months she had had edema of the lower extremities, chronic headache, fainting spells and blurring of vision. She had 3 children, all delivered normally, but in 2 subsequent pregnancies she was hospitalized with the same complaint as on this admission. Both resulted in premature stillbirth deliveries. Ophthalmoscopic examination revealed marked arteriovenous compression. There were fine moist rales in the bases of both lungs. A soft, blowing systolic murmur was heard in the mitral area and over the pulmonic region. The urine showed a trace of albumin on several occasions, but no casts. The blood pressure was 230/115.

Placed on a regime consisting of 20 per cent glucose, and 10 per cent magnesium sulfate intravenously, sedation and strict bed rest, the patient improved considerably; the blood pressure decreased to 140/110. Approximately 17 days after admission to the hospital she awakened in severe pain. Examination revealed moderate tenderness of the epigastrium but no spasm or rigidity. The blood pressure could not be obtained, the pulse was rapid and thready and fetal heart tones were inaudible. A diagnosis of internal abdominal hemorrhage was made, but before surgery could be performed, death occurred, 7 hours following the onset of severe abdominal pain.

Autopsy revealed an irregular tear 5.0 cm. long on the anterior surface of the spleen and about 1500 cc. of fresh blood and clots in the abdominal cavity. A thrombus was attached to the wall of the splenic artery. The chief pathological findings were in the abdominal cavity and heart.

None of the usual etiological processes associated with splenic thrombosis was observed in this case. It is suggested that the reduction of blood pressure and the stasis resulting from barbiturates may have contributed to thrombosis of the splenic vein.

## THE MEDICAL MANAGEMENT OF INCOMPLETE ABORTION

FRED B. NUGENT

Pennsylvania M. J., 49: 523-524, 1946

The chief dangers of incomplete abortion are hemorrhage and infection. The recognized methods of combatting hemorrhage and its sequelae are evacuation

## SPONTANEOUS RUPTURE OF THE LIVER COMPLICATING PREGNANCY

HAROLD LINKS

Brit. M. J., 1: 275-276, 1946

Only one case of spontaneous rupture of the liver complicating pregnancy can be found in the literature. This was reported by Rademaker in 1943. The patient was 8 months pregnant when she suddenly developed signs of toxemia with albuminuria and a blood pressure of 240/160. After a bout of vomiting she showed signs of hemorrhage and an operation was performed, during which lacerations in the liver were found and packed. The patient recovered. In Rademaker's opinion, the high blood pressure and sudden muscular effort caused the rupture of hepatic vessels.

The author presents the case of a 42 year old woman who was admitted to the hospital with an "acute abdomen". The history was essentially negative and the present pregnancy was of 16 weeks' duration. Twelve hours before admission she experienced sudden violent abdominal pain which was localized to the right hypochondrium and was so severe as to cause collapse.

On examination there was generalized abdominal tenderness without rigidity but with relative resistance of the right upper rectus muscle. On percussion, shifting dullness was present; the area of hepatic dullness was normal. The pulse was of poor volume, the rate 140 per minute; the temperature was 99.4 degrees, and the blood pressure 110/70. Urinary examination revealed a specific gravity of 1020 and no abnormal chemical constituents. A preoperative diagnosis of hemoperitoneum, probably due to a gynecological cause, was made.

A blood transfusion was begun and an operation was performed. On opening the abdomen the peritoneal cavity was found to be filled with blood. No cause for the hemorrhage could be found in the uterus or adnexa. Clots were seen in the right hypochondrium and blood was coming through the foramen of Winslow. The gastro-hepatic omentum was incised and a blood clot was found in the lesser sac. A transverse rupture, 5 cm. in length, was located in the caudate lobe of the liver. The rupture was plugged with a piece of the right rectus muscle and the abdomen was closed. Transfusion was continued and the patient made a rapid recovery. She miscarried 5 days after operation but suffered little ill effect. She was discharged 23 days postoperatively; the wound was soundly healed and she was symptom-free.

The etiology of this case is very obscure. Even after the massive hemorrhage the patient still had a systolic blood pressure of 110 mm. Hg. Further note may be made of the apparent discrepancy between this blood pressure reading and the rapid feeble pulse and profound state of shock. It is suggested that she might have been hypertensive before the rupture occurred, and that this hypertension superimposed on the hyperemic pregnant liver causing rupture of the organ.

macerated fetus, probably the result of a syphilitic infection, 4 weeks after treatment. A third patient noted vaginal bleeding about 5 weeks after treatment when she was about 34 weeks' pregnant, but proceeded uneventfully to term. A fourth patient delivered a child of 36 weeks' gestation 4 weeks after treatment. The fifth patient delivered after 34 weeks' gestation and at this time showed evidences of toxemia of pregnancy. She had received penicillin treatment 20 weeks previously.

Three patients delivered during the course of penicillin therapy; 2 of these were at term. The third patient delivered during treatment after a 30 weeks' gestation. She subsequently aborted after a 20 weeks' gestation and later developed infectious syphilitic lesions. Only in this case can there be any question regarding the possible effects of penicillin treatment upon the pregnant uterus, and here it is highly doubtful.

Alteration in menstruation during the course of penicillin therapy also has been reported. The authors have given penicillin to over 1300 women without ever noting any menstrual abnormality attributable to such therapy. They have accurately studied 100 patients under treatment for early syphilis with penicillin and in only one instance was any alteration from the usual cycle noted.

of the uterus, packing, oxytocics, and intravenous infusions of blood, plasma or other blood substitutes. For the control of infections the value of the sulfonamides and penicillin is unquestioned. However, the importance of supportive measures such as frequent small transfusions, Fowler's position to facilitate downward drainage, adequate rest and careful attention to nutrition and elimination should not be forgotten.

A series of 300 consecutive cases of incomplete abortion has been divided into 4 readily recognized groups, with detailed suggestions as to the management of each group. This classification may be summarized as follows:

Group I.—Obviously clean cases with the placenta presenting in the cervix.

Group II.—Obviously clean cases in which the secundines were not presenting.

Group III.—Patients in whom infection was suspected or present to a mild degree.

Group IV.—Patients with obviously severe infections.

This classification may assist the busy practitioner of medicine in dividing his cases into those which require hospitalization and those which do not. Fifty-three per cent of the patients in Groups I and II could have been treated as successfully at home as in the hospital.

(Certainly the patients in whom infection is suspected or obvious are much more safely treated in the hospital than in the home, in spite of the fact that these are the ones in whom surgical invasion of the uterus is ordinarily contraindicated, except in the presence of serious bleeding. In the latter, gentle evacuation of the uterus may be necessary. In the clean cases, hemorrhage likewise may necessitate emptying the uterus, by means of the ovum forceps, finger or dull curette.—Ed.)

## REGARDING THE UNUSUAL EFFECT OF PENICILLIN THERAPY UPON THE UTERUS

M. D. SPEISER AND E. W. THOMAS

*J. Vener. Dis. Inform.*, 27: 20-21, 1946

The authors have reviewed the records of 156 prenatal patients treated with penicillin in the Rapid-Treatment Center at Bellevue Hospital in order to evaluate previous reports that penicillin therapy has caused some pregnant women to experience uterine contractions which in a few cases resulted in abortion. The patients studied in this paper received penicillin in amounts varying from 600,000 to 2,400,000 Oxford units.

There were 5 patients who showed some aberration from the usual course at a variable time after penicillin treatment, but in none of these instances could a possible relationship between penicillin therapy and the alteration in the course of the pregnancy be suspected. One patient aborted 2 to 3 weeks after discharge at about the eighth week of pregnancy. A second patient delivered a 28 weeks'

Placenta previa is another stated factor in breech births. Only 8 cases of placenta previa were recorded in 677 breech births.

Pelvic tumors, reputed to cause breech presentation, were mentioned in only 4 of the 677 case histories, accounting for 0.6 per cent of all breeches observed.

Uterine anomalies, particularly bicornate uterus, are often associated with faulty presentation. Four cases were observed in the present series, and there was one case of septate vagina which may have been accompanied by a divided uterus.

An examination was made of 100 records chosen at random of patients who had 2 cesarean sections to determine the influence of a uterine scar on breech presentations. Only one patient had a breech lie when the second cesarean was performed.

Odell and Mengert report 5.5 per cent breeches (over 1500 grams) among 687 deliveries of patients who weighed 200 or more pounds. If this percentage in-

TABLE IX

*Showing that the classical explanations for breech presentation account for only 15 per cent of breeches observed*

	BABIES OVER 2,500 GRAMS		BABIES UNDER 2,500 GRAMS	
	No.	%	No.	%
"Contracted pelvis".....	75	11.1	24	10.2
Gross fetal anomalies.....	11	1.6	10	4.3
Placenta previa.....	8	1.2	9	3.9
Pelvic tumors.....	4	0.6	1	0.4
Uterine anomalies.....	4	0.6	2	0.8
No demonstrable factor.....	575	84.9	188	80.3
Totals.....	677	100.0	234	100.0

cludes twins and babies delivered after internal podalic version, the incidence of breech presentations among obese patients is not remarkably high.

In fairly examining the question of maternal age as a factor in breeches, the effect of multiparity on breeches must be eliminated and data from elderly primiparas only considered. The incidence of breeches in primiparas of 35 years and over in this clinic is 9 per cent. It seems not improbable that older primiparas have a somewhat greater tendency to breech presentations.

It would be difficult to determine the role of polyhydramnios in producing breeches. The relation of polyhydramnios to breech presentations depends not so much upon the measurable amount of fluid but upon the relation between the volume of the fluid and the volume of the baby.

The more commonly accepted etiological influences are listed in Table IX. It may be seen that only 15 per cent of breech births of mature single babies has been accounted for. Therefore, it is clear that other factors than those classically recognized must be involved.

Fetal activity is seldom mentioned in the etiology of presentation. However,

## **PATHOLOGY OF LABOR AND PUERPERIUM**

### **AN INQUIRY INTO THE CAUSES OF BREECH PRESENTATION**

PENDLETON TOMPKINS

*Am. J. Obst. & Gynec.*, 51: 595-606, 1946

In this paper, the author considers 2 aspects of the etiology of breech presentation. First, he examines the "classical factors" usually alleged to cause breech presentation and second, he considers other unrecognized factors.

At the Philadelphia Lying-In Hospital in the 10 years following January 1, 1933 there were 1184 breeches among 25,170 deliveries. Excluding breech deliveries after internal podalic version and excluding all twins presenting by breech, there remain 911 single "primary" breech presentations delivered normally or by cesarean section. Multiple pregnancy is excluded from the study proper. It would be expected that twins would lie in utero in a head-to-breech position, each facing medially with relation to the mother, and multiple pregnancy undoubtedly disposes to the breech presentation of one baby.

Prematurity is an important feature in breech presentation, since breeches are common until the last month or so of pregnancy and spontaneous version to cephalic presentation is the rule as term approaches. Therefore, in order to determine the mechanism producing breeches at term, one must separate the premature babies arbitrarily from the mature. Most of this study is therefore concerned with single pregnancies terminating in a breech baby weighing 2500 or more grams.

Multiparity is a stated cause of breeches. As a preliminary study of the effect of multiparity, the incidence of breeches was determined in groups of primiparas, secundiparas, and so on. The results show that multiparity is not of particular importance as a cause of breech presentation.

It appears that some patients have an individual tendency to bear breech babies. Also, a report by Cartledge and Hancock suggests a hereditary tendency to breech.

Contracted pelvis is an old and not very sound explanation for breech presentations. Among mothers bearing 677 mature breech babies, 11 per cent had "contracted pelvises." Of all the breech deliveries observed, 89 per cent could not be attributed to contracted pelvis.

Gross fetal abnormalities are often associated with breeches. Data collected by Young and Potter on a series of 1705 malformed fetuses and infants show that 26 per cent of hydrocephalics and 18 per cent of anencephalics weighing over 2500 grams delivered as breeches. Therefore, fetal abnormalities predispose in some way to breech presentation. However, neither hydrocephalus, anencephalus nor other gross abnormalities play a very great part in producing breech lies in a large series of breeches; among 677 breech babies over 2500 grams in the present series, there were only 7 hydrocephalics and 2 anencephalics.

few years he will be prepared to report current experiments which deal with the effects of gravity and of the contour of the fetal mass upon polarity.

(See editorial note in the April issue of the Survey, page 193.—Ed.)

## UTERUS DIDELPHYS AND ITS CLINICAL SIGNIFICANCE IN PREGNANCY

EDWIN S. HOFFMAN

*Am. J. Obst. & Gynec.*, 51: 692-698, 1946

The degree of duplicity of the uterus, cervix and vagina depends entirely upon the degree of failure of fusion of the Müllerian ducts; "complete uterus didelphys" is the result of complete lack of fusion of the Müllerian ducts. As a rule, uterus didelphys is of no clinical significance except in pregnancy, and no special treatment is needed unless the patient complains of dyspareunia or unless the abnormality is associated with pelvic disease or tumor.

Pregnancy may occur in association with uterus didelphys. Some cases have been reported in which pregnancy occurred simultaneously or at different times in both uteri. The author advises close prenatal supervision with careful pelvic measurements including x-ray pelvimetry.

During pregnancy, abortion, premature labor, abruptio placentae and premature separation of the placenta are more common than in the absence of uterus didelphys. Should premature separation of the placenta or premature labor occur, one should be prepared, if necessary, to do an abdominal section.

During labor, maternal exhaustion, fetal embarrassment, prolonged first stage of labor, rupture of the uterus, and dystocia caused by the nonpregnant uterus may occur. Interference by the nonpregnant uterus may result in oblique and other abnormal presentations. Operative deliveries may result in increased fetal morbidity and mortality. Whenever advisable, a test labor should be given, the obstetrician being prepared to do a cesarean section if dystocia or fetal embarrassment should occur. Cesarean section will eliminate maternal exhaustion, prolonged labor, undue complications, and decrease fetal and maternal mortality and morbidity. In certain cases elective cesarean section will be the operation of choice. The author believes that it is more conservative to do an elective cesarean than to submit the patient to unnecessary risks. Uncomplicated delivery will occur in many cases and the milder forms of uterus didelphys will probably cause no trouble.

Following labor, postpartum hemorrhage, retained placenta and subinvolution may occur. None of these complications was observed in the present series of 6 cases.

(Hoffman is entirely correct in stating that cesarean section is sometimes justified in

if one inquires about the degree of fetal activity at each antepartum visit, it will be noted that when relative inactivity is reported the baby is often found in a breech presentation. It is reasonable to believe that maimed babies who have impaired powers of motion, and babies whose movement is limited by extension of the legs, would have less chance of extricating themselves from a breech lie by their own efforts than vigorous babies with flexed legs.

Vartan has developed the idea that extension of the legs might be a primary cause of breech presentations. When his data are compared with the author's and both are tabulated, some 60 per cent of breeches are explained, whereas the "classical factors" account for only 15 per cent. To determine the incidence of extended legs in cephalic presentations the writer reviewed a random group of x-ray films taken at or near term. Of 123 films examined there were 96 in which the legs were clearly visible. Four of these were breech presentations in which all had extended legs. The remaining 92 were cephalic presentations and of these, 89, or 97 per cent, had both legs flexed at the knee. The remaining 3, or 3 per cent, had one or both legs extended at the knee.

Cord complications, such as short cords, or coils of cord around the extremities, may account for some breeches by interfering with spontaneous version. Prolapse of the cord occurred in 15 of the 677 breech deliveries, but not once among the frank breeches (which constituted two-thirds of all breeches delivered). If it could be shown that the slack length of cord was decreased by being coiled about the body or extremities, we should have a possible explanation both for the breech lie and for the absence of prolapse.

From these data the author presents a hypothetical explanation of breech presentations. As pregnancy progresses the shape of the uterine cavity changes from spheroid to void and at the same time the center of gravity and the center of buoyancy of the fetus are altered so that it tends to lie head downward rather than breech downward. If labor occurs when the fetus attains 1500 grams, the factors influencing polarity produce a breech presentation in about one-sixth of the cases delivered. The typical "fetal attitude" at this time is one of extreme flexion and any motions must be toward a position of extension. Should the amniotic fluid suddenly escape and the uterus contract, the fetus will be delivered in his presentation of the moment.

If premature labor does not occur, it may be that, at term, there is interference with fetal movements or that the contour of the uterus is not ovoid. In the former case, spontaneous podalic version may be impossible because the cord is coiled about the body or extremities and the fetus is either tied in a given position or the entangling cord limits leg movement. In rare instances, the uterus itself may be faulty, as in the case of a septate or a bicornate uterus.

In still other cases the fetus is at fault. As a result of hydrocephalus, meningocele, dysplasia of the hips, cerebral agenesis, or some other congenital defect, its intrauterine vigor may be impaired.

The mechanism by which extension of the legs may operate to affect the presentation is not fully discussed in this paper. It is the writer's hope that within a

Once a patient had had a vaginal delivery following cesarean section, the greater was the probability of future vaginal deliveries. The converse was also true; the greater number of cesarean sections a patient had had, the less the chance of vaginal delivery. The greatest number of vaginal deliveries occurring in one patient following previous section was 8, and the greatest number of sections performed on one patient was 6.

In the majority of sections for disproportion, the indication is relative to the powers of labor, position and pelvic configuration. This is demonstrated by both clinical and x-ray pelvimetry. For this reason, x-ray pelvimetry can rarely provide an absolute indication for section.

An unusually high incidence of abnormal presentations may be explained on the basis of poor pelvic architecture.

It is important to examine the scar of the previous cesarean section at the time of operation or vaginal delivery for better evaluation of succeeding pregnancies. Defects in the uterine scar were noted more frequently following the classical type of section. In one-half of the cases where there was a defect in the uterine scar, it was suspected prior to operation. However, in only one-third of the patients in whom section was performed on the indication of damage to the uterine wall, were any defects noted. Rupture of the previous scar occurred in 1.3 per cent of the patients in this series. There were no maternal deaths among these patients; the author believes this to be attributed to close observation and prompt action.

The high morbidity (29 per cent) is explained by the high operative incidence.

The fetal mortality rate was 6.9 per cent. There were 3 maternal deaths, a mortality rate of 0.67 per cent.

## RUPTURE OF THE UTERUS

GARIPUY, PONTONNIER AND FERRIER

Gynec. et obst., 44: 393-94, 1945

This case report deals with a 39 year old woman with the following obstetric history: simple forceps delivery of a normal infant 19 years prior to the present report; a spontaneous delivery 5 years later; in 1940 an abortion in the 2nd months, followed by curettage.

In the present instance, the patient was admitted to the hospital in labor at 3:00 A.M.; the labor appeared to be progressing normally. At 10:30 A.M., dilatation being almost complete, an injection of  $2\frac{1}{2}$  units of posterior-pituitary was given. At 11:00 A.M., dilatation was complete and another injection of  $2\frac{1}{2}$  units of posterior-pituitary was given. At this time the uterine contractions ceased and the patient complained of pain in the left side. A small projecting mass was felt on the left side which was interpreted as a subserous fibroma. There were no signs of hemorrhage or shock. Auscultation was negative.

patients with uterus didelphys because of the several complications he mentions. However, it is difficult to forecast beforehand just how labor will progress in these patients. Some do beautifully with short easy labors, while others go in for intractable uterine inertia and occasionally, of course, the non-pregnant horn may block the birth canal. A few years ago a patient was referred to us after 48 hours of futile labor who gave a history of having lost her last 4 babies because of 3 and 4 day labors. At cesarean section a uterus didelphys was found. Our very next patient with this deformity, on the other hand, had an easy 10 hour labor. It seems to me, accordingly, that unless the non-pregnant horn blocks the birth canal or unless there is a history of infant loss in previous labors, all these patients should be given a trial labor of 15 hours or so before deciding about method of delivery. —Ed.)

## DELIVERY AFTER CESAREAN SECTION

FLORENCE A. DUCKERING

Am. J. Obst. & Gynec., 51: 621-634, 1946.

The present study covers a 12-year period from September 1, 1932, to December 31, 1943, and consists of 445 viable pregnancies following a previous cesarean section.

The chief indication for previous cesarean section was disproportion. The majority (57 per cent) of previous sections were of the classical type.

Fifty-eight per cent of the patients in this series were delivered by another cesarean section. About two-thirds of these were classical sections and one-third were low flap. The greatest number of repeat sections occurred in the group where disproportion had been the indication for previous cesarean section. Among patients in whom the original indication was no longer present in the succeeding pregnancy, the number of repeat sections was lowest. Forty-two per cent of the patients were delivered vaginally; slightly more than one-half of the vaginal deliveries were operative, and the remainder spontaneous.

Among those patients delivered by repeated section, a large proportion (25.8 per cent) were indicated because of a defective uterine scar or febrile puerperium. There was a high incidence of premature separation of the placenta and placenta previa in this group of patients requiring another section.

In cases of vaginal delivery, a routine low forceps is considered the procedure of choice after a previous section.

The most marked variation in incidence of vaginal deliveries following cesarean section was found in the group where previous section was performed for the indication of disproportion, as compared with that group in which disproportion did not enter into the original indication. Of 253 previous sections for disproportion, 31.7 per cent had a vaginal delivery at this time. Among 124 patients who had previous sections for severe pre-eclampsia, abnormal presentation, desultory labor, and other abnormalities which are not likely to be present in succeeding pregnancies, 58.9 per cent delivered vaginally.

Of 253 repeat sections, 76.3 per cent were elective, and the remainder were allowed to go into labor. The average trial of labor lasted 10 hours and 48 minutes.

eralized and symmetrical swelling of the abdomen. Examination of the hernial orifices was negative and no abdominal scars were noted. The fetus was located by x-ray and lay in a vertical position in the midst of greatly distended intestines. Duodenal aspiration was begun immediately but the symptoms did not subside. At laparotomy the peritoneum appeared bluish and a large mass of clotted blood was found; the fetus was dead. The uterus was exteriorized and a rupture was found situated horizontally at the site of the previous curettage. It was located on the posterior surface of the organ and above a fibroma the size of a hen's egg. Hysterectomy and peritonization were performed and the patient made an uneventful recovery. A noteworthy feature of this case was the almost total absence of shock and signs of internal hemorrhage which led to an error in diagnosis. On admittance to the hospital her temperature had been 37 degrees C., pulse 80 and respirations 22.

(The best guess in this case would be that the uterus was perforated at the previous curettage.—Ed.)

## TWO OBSERVATIONS OF SPONTANEOUS RUPTURE OF THE UTERUS DURING PREGNANCY

DUJOL, PELLISSIER, MICHELLAND AND MICHE

*Gynéc. et obst.*, 44: 376-78, 1945

The first case presented is that of a 29 year old woman who had a spontaneous rupture of the uterus in the 6th month of her 2nd pregnancy. Curettage had been done 10 years previously and an appendectomy had been performed during the 2nd month of her present pregnancy. After the latter operation the patient continued to complain of abdominal pain, nausea and vomiting until during the 4th month of the pregnancy. In the 6th month she experienced a sudden, violent attack of abdominal pain which was diagnosed as hepatic colic by one physician and as peritoneal inundation by another. On examination in the hospital, the patient presented a severe hemorrhagic syndrome and grave anemia. There was no collection of blood in the vagina. On opening the peritoneum, the fetus and placenta were located in the abdomen which was filled with blood. The uterus was wide open at the base, but no longer bled. A subtotal hysterectomy was performed but the patient died 3 weeks later from infection. The entire base of the uterus consisted of fibrous, extremely fine scar tissue which did not exceed a half centimeter in thickness at the level of the rupture. The rupture itself was 10 to 15 cm. long and extended transversely between the two horns but did not reach them.

In the 2nd case, the rupture occurred during the 7th month of the 6th pregnancy in a 32 year old woman who had no history of previous obstetrical intervention. One pregnancy had terminated in a stillbirth at term and another in a spontaneous abortion at 3 months, for which no subsequent treatment was re-

Forceps were applied under chloroform and a dead female infant was delivered. The death of the child could not be explained. Because of the abnormal character of the delivery and because of the bizarre aspect of the uterus with its lower segment enlarged and the palpation of a tumefaction on the left side, laparotomy was performed. Blood was found in the peritoneal cavity and on the left lower segment of the uterus a rupture was discovered which extended to the body of the uterus. As the fetus had already passed this point before the application of the forceps, it was concluded that the instrumental delivery was not responsible for the rupture. The absence of hemorrhage led the authors to believe that this was a rupture of scar tissue, probably dating back to the curettage performed in 1940.

(Although the original article has been carefully scanned, the fact that the uterine rupture might (!) have been due to the pituitary extract is not so much as mentioned and was apparently not even suspected.

The most convincing evidence in this case that rupture occurred prior to forceps application was the sudden cessation of labor at full dilatation and one hour before the instruments were employed. Particularly in a multipara this should always suggest rupture. The sudden cessation of labor plus the disappearance of the fetal heart sounds pointed, of course, all the more strongly to rupture.

The observation that shock and hemorrhage were minimal does not necessarily mean rupture of scar tissue since rupture of the intact uterus may occasionally be silent. In 17 spontaneous (non-caesarean) ruptures of the uterus seen at the Johns Hopkins Hospital, shock was present in only 9 and vaginal bleeding in 15. This fact that spontaneous rupture of the intact uterus may occasionally occur without shock or hemorrhage needs continual re-emphasis because failure to bear this point in mind has resulted so many times in long and often fatal delays in making the diagnosis. In our 10 post-caesarean ruptures, shock was observed in only 3 cases and external bleeding in only one.—Ed.)

## SPONTANEOUS RUPTURE OF THE UTERUS AT THE EIGHTH MONTH WITH MISLEADING SYMPTOMATOLOGY

E. LÉVY-SOLAL, P. MORIN AND F. HANON

*Gynéc. et obst.*, 44: 323-24, 1945

The subject of this case report was a 30 year old woman, 3-para. Her first pregnancy terminated in spontaneous abortion in the 3rd month. The 2nd pregnancy likewise terminated in abortion at 2.5 months and necessitated curettage. No abnormal sequelae were noted. The present pregnancy followed a normal course until the end of the 7th month when the patient began to complain of acute hypogastric pains at about hourly intervals for one day. The next day she did not feel pain. The following day, however, the pains returned and were accompanied on the 4th day by diarrhea and gas. The pains were intermittent for the next 2 days. Active fetal movements were felt until the 5th day. There was no external hemorrhage. On the 6th day the patient was admitted to the hospital in a state of extreme agitation, intense superficial dyspnea and a gen-

catheter inserted since she was unable to urinate. Reposition of the cervix was again tried and failed and a line of demarcation appeared at the level of the constriction; gangrene was apparent. The gangrenous portion of the cervix was removed by a diathermy knife and eventually, after a somewhat stormy convalescence, the patient was discharged. Examination prior to discharge showed the absence of pus discharge and a slight cystocele with some laxity of the posterior vaginal wall. The cervix was flush with the vaginal vault, the uterus was well involuted and the parametria were clear.

It is suggested that this prolapse was caused by a sudden bearing down effort of the patient after the birth of the baby with an irreparable damage to the uterine ligaments which immediately caused descent. These ligaments are attached to the uterus at the level of the internal os in a circular fashion forming what is known as the "fixation circle." During the expulsion of the fetus the fixation circle descends to some extent without damage to the ligaments. However, while the fixation circle is gradually going up after expulsion of the fetus, a sudden bearing down effort on the part of the patient could cause great damage to the ligaments.

## A CASE OF CLOSTRIDIUM WELCHII PUERPERAL INFECTION TREATED WITH PENICILLIN

R. B. GOLDBERG AND W. K. KONIGSBERG

Am. J. Obst. & Gynec., 51: 527-532, 1946

Since the first report of puerperal infection due to *Clostridium welchii* by Dobbin in 1897, many cases have been described. The importance of the early diagnosis of severe gas bacillus infections with their rapidly fatal outcome in most untreated cases is obvious. Once the diagnosis is established, supportive and specific therapy must be begun without delay. In the present paper, the authors present a case of moderately severe postabortal puerperal infection with *Cl. welchii* which was successfully treated with penicillin given intramuscularly in a total dosage of 1,200,000 units.

The patient, a 30 year old nurse, entered the hospital because of premature rupture of the membranes and a pregnancy of 6 months' duration. She was not in labor. Approximately 9 months previously her first pregnancy had ended in the spontaneous expulsion of a 4½-month fetus.

In the hospital, the patient leaked amniotic fluid for 5 days before abortion occurred. On the day of abortion the temperature was elevated for the first time but remained essentially normal throughout the height of the subsequent infection. Within 24 hours the patient was markedly jaundiced, superimposed on which was a cyanotic hue, especially evident in the lips and nailbeds. She became toxic and lethargic. Other clinical features were: (1) a high white blood count with a marked shift to the left; (2) port wine urine; (3) a sharp drop in

ceived. In the 3rd month of the present pregnancy she had a hemorrhage. Another hemorrhage in the 7th month was accompanied by abdominal pain. Anticipating a premature birth, the physician prescribed rest in bed. However, 3 days later she was brought to the hospital in a comatose state. It was thought that this was a case of premature separation of the placenta. The abdomen was found to be filled with blood and a dead, but not macerated, fetus lay in the midst of the intestines. The uterus had partly retracted upon itself and, on the left posterior surface, presented a slightly open rupture about 14 to 15 cm. in length. The edges were not bleeding. A rapid hysterectomy was performed. In spite of blood transfusions the patient died. Examination of sections taken from the region of the rupture showed the presence of inflammatory signs, such as perivascular discs and a discrete infiltration of polynuclear cells and lymphocytes. In the muscular wall there was a large area in which the muscle fibers seemed to show the beginning of degeneration of fatty tissue in the form of young fatty cells which had replaced the muscular tissue. Fatty degeneration of the uterine wall in cases of rupture has been observed by several authors.

(Spontaneous, non-cesarean rupture of the uterus in pregnancy is the rarest of the rare but the latter case in particular would seem to fall into this category.—Ed.)

## PROLAPSE OF UTERUS FOLLOWING NORMAL LABOUR

KALYAN KUMAR GHOSAL

J. Indian M. A., 15: 120-121, 1946

The case is presented of a 30 year old woman who was admitted to the hospital after confinement at home with the complaint that the womb had come down after the birth of the child and expulsion of the placenta. Labor had been normal and the placenta was naturally expelled half an hour after the child's birth. Following the expulsion of the placenta there was a small hemorrhage and the placenta was thought to be incompletely expelled. The patient was asked to sit up and bear down and with this, the uterus suddenly descended so that the entire cervix protruded from the vulva. The patient developed severe shock and was brought to the hospital.

The previous history revealed no evidence of symptoms relating to a weakening or laxity of the pelvic floor. The patient had had 9 pregnancies, 3 of which ended prematurely. The previous labors and puerperia had been normal.

On examination, her general condition was poor and the cervix, which wholly projected from the vulva, was enormously swollen, edematous, raw and bleeding. When the patient's general condition had been somewhat improved, reposition of the cervix was attempted under anesthesia, but failed because of the bulk of the cervix and friability of the tissues.

Her temperature varied from 99 to 102°F., the urine on culture showed colon bacillus and anemia increased. Sulfathiazole was given and a self-retaining

catheter inserted since she was unable to urinate. Reposition of the cervix was again tried and failed and a line of demarcation appeared at the level of the constriction; gangrene was apparent. The gangrenous portion of the cervix was removed by a diathermy knife and eventually, after a somewhat stormy convalescence, the patient was discharged. Examination prior to discharge showed the absence of pus discharge and a slight cystocele with some laxity of the posterior vaginal wall. The cervix was flush with the vaginal vault, the uterus was well involuted and the parametria were clear.

It is suggested that this prolapse was caused by a sudden bearing down effort of the patient after the birth of the baby with an irreparable damage to the uterine ligaments which immediately caused descent. These ligaments are attached to the uterus at the level of the internal os in a circular fashion forming what is known as the "fixation circle." During the expulsion of the fetus the fixation circle descends to some extent without damage to the ligaments. However, while the fixation circle is gradually going up after expulsion of the fetus, a sudden bearing down effort on the part of the patient could cause great damage to the ligaments.

## A CASE OF CLOSTRIDIUM WELCHII PUERPERAL INFECTION TREATED WITH PENICILLIN

R. B. GOLDBERG AND W. K. KONIGSBERG

Am. J. Obst. & Gynec., 51: 527-532, 1946

Since the first report of puerperal infection due to *Clostridium welchii* by Dobbin in 1897, many cases have been described. The importance of the early diagnosis of severe gas bacillus infections with their rapidly fatal outcome in most untreated cases is obvious. Once the diagnosis is established, supportive and specific therapy must be begun without delay. In the present paper, the authors present a case of moderately severe postabortal puerperal infection with *Cl. welchii* which was successfully treated with penicillin given intramuscularly in a total dosage of 1,200,000 units.

The patient, a 30 year old nurse, entered the hospital because of premature rupture of the membranes and a pregnancy of 6 months' duration. She was not in labor. Approximately 9 months previously her first pregnancy had ended in the spontaneous expulsion of a 4½-month fetus.

In the hospital, the patient leaked amniotic fluid for 5 days before abortion occurred. On the day of abortion the temperature was elevated for the first time but remained essentially normal throughout the height of the subsequent infection. Within 24 hours the patient was markedly jaundiced, superimposed on which was a cyanotic hue, especially evident in the lips and nailbeds. She became toxic and lethargic. Other clinical features were: (1) a high white blood count with a marked shift to the left; (2) port wine urine; (3) a sharp drop in

hemoglobin and red count; (4) hemoglobinuria; and (5) positive uterine culture of *Cl. welchii*. Some 34 hours after abortion penicillin therapy was begun and 6 hours later the patient was clinically improved. Convalescence was slow with the later development of uremia, hypertension and tetany, but the patient recovered.

It is suggested that combined penicillin and specific antitoxin therapy might be more rational and potentially more effective.

## PUERPERAL INFECTION; ETIOLOGIC, PROPHYLACTIC, AND THERAPEUTIC CONSIDERATIONS

R. G. DOUGLAS AND I. F. DAVIS

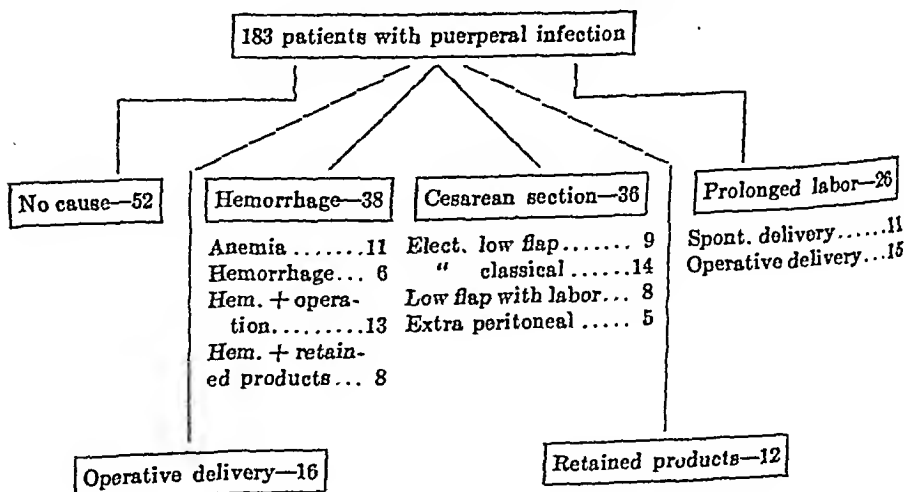
Am. J. Obst. & Gynec., 51: 352-371, 1946

The author presents evidence which indicates a decreased puerperal infection mortality in the United States, amounting to approximately 50 per cent during recent years, as compared to previous experience, while in New York City these rates remain essentially the same, despite a decrease in total maternal mortality during the past decade to one-third the former rate. In the New York Lying-In Hospital both the incidence of puerperal infection and the mortality associated with this condition have shown a progressive and very significant decrease.

The bacteriologic data obtained from the study of 1000 patients subjected to investigation indicate that the great majority of infections occurring during the puerperium and postabortal period are endogenous in origin, and are caused for the most part by different groups of nonhemolytic streptococci.

An analysis of underlying conditions responsible for the development of infection reveals the following information:

*Underlying causes of puerperal infection,  
New York Lying-In Hospital—1944*



It is shown that prophylaxis of infection is far more important than the treatment of the disease once established. Endogenous infections constitute by far the largest group encountered and are the most difficult to control. The organisms are present in the vagina at the beginning of labor. Observations of patients with normal and prolonged labor indicate that the process of infection actually begins with the onset of labor in every patient. It is apparent that the most rigorous application of aseptic principles will not necessarily prevent infection. The incidence of infection can be greatly reduced if, in addition to strict aseptic principles, the following conditions are fulfilled:

1. Anemia is successfully treated during pregnancy.
2. Excessive blood loss (or anemia) is restored immediately post partum, irrespective of the development of shock.
3. Prolonged labor is anticipated when indicated, and analgesics employed judiciously in such circumstances.
4. Trauma is minimized.
5. Cesarean section, with rare exceptions, should be performed electively or after not more than 8 to 12 hours of labor.
6. Lacerations are repaired with the application of accepted surgical principles.
7. Retained portions of the placenta are removed immediately after completion of the third stage of labor.
8. Operations are properly timed and restricted to those patients with adequate indications.
9. Intercurrent disease should be eliminated or controlled, if possible, before the onset of labor.

It is the authors' opinion, based on experience but not proved conclusively, that sulfadiazine, given early during long labors and under certain other circumstances, will decrease the incidence of infection. In the treatment of puerperal and postabortal infections, sulfadiazine or penicillin given early may be efficacious, while late in the course of the disease they may be relatively ineffective.

Several shortcomings in therapy may be summarized as follows:

1. Failure to recognize intrapartum and postpartum infection early, which delays treatment.
2. Underestimation of blood loss and failure to give prophylactic transfusions when indicated.
3. Failure to recognize signs of peritonitis which are often called distention, paralytic ileus, acute dilatation of the stomach, etc., which consequently delays therapy.
4. The performance of cesarean section after many hours of labor.
5. Late commencement, inadequate dosage and alternation of different compounds in sulfonamide therapy.
6. Discontinuance of sulfonamide therapy because of symptoms of the disease interpreted as evidence of toxic reactions.

Individual case records are presented which illustrate the considerations set forth in this paper.

## THE NEWBORN

### MARRIAGE AND CHILDREN FOR EPILEPTICS

WILLIAM G. LENNOX

Human Fertil., 10: 97-106, 1945

The question of whether marriage and children are advisable for epileptics has been one of some dispute. The author states that "it is high time that available present-day information on this subject should be substituted for tradition and gossip."

Both in making a differential diagnosis and in helping to estimate the future when marriage is considered, a well made electroencephalogram is of great value to the physician. For the purposes of advice, the type and degree of abnormality are important.

Seizures are not influenced in any uniform manner by marriage, pregnancy or child bearing. If the marriage is happy and the pregnancies uncomplicated, an epileptic wife may be better than formerly. Epilepsy is a potential economic burden and is also a social and psychological hazard. It is better to have genetic epilepsy than acquired epilepsy, for brain damage greatly complicates the prognosis.

Based on family histories, the hereditary factor in epilepsy is about the same as in diabetes, one-half that in obesity and one-eighth that in migraine. The chance that any given child of an "average" epileptic will also be epileptic is about one in 40. Following are the various factors which, if present, make a child's chance of not having seizures greater than 39 out of 40, boosting it to 99 out of 100 or above.

(1) If acquired factors, such as a history or evidence of brain injury, contributed to the patient's epilepsy.

(2) Absence of epilepsy or migraine among blood relatives and, when obtainable, relative good brain wave records of parents.

(3) Seizures which began later than infancy or childhood. The earlier that the symptoms appear the greater is the hereditary factor unless there was an early acquired injury to the brain.

(4) Normal mentality of the patient at birth.

(5) Probably the most important factor is the absence of a predisposition to seizure in the spouse, as evidenced by a family tree free of epilepsy or migraine and a brain wave record which is normal. The marriage of 2 normal persons who both carry a predisposition to seizures is worse than the union of an epileptic with a person who has no predisposition.

Epilepsy is characterized by a dysrhythmia of the electrical potentials of the brain. Electroencephalograms have been made of twins, both normal and epileptic, and of parents and other near relatives of epileptics, to a total number

of 675. Study of these tracings leads to the conclusion that the brain wave pattern is an hereditary trait, and the electroencephalogram, when properly made and interpreted, may be used in studying the heredity of epilepsy and as an aid in advising about marriage and children. The evidence indicates that epilepsy, *per se*, is not inherited but a predisposition may be.

The degree of electroencephalographic abnormality is doubtlessly important. An acquired dysrhythmia must be distinguished from one which is transmitted. Conditions associated with developmental abnormalities of the brain (such as mongolism, microcephalus, amentia, or feeble-mindedness) may be, but usually are not, accompanied by slowing of the dominant rhythm. In trauma to the brain at or after birth, in infections or in tumor, slowing of the wave is usual. In the presence of acquired pathology, certain types of seizure discharge predominate.

If a person has dysrhythmia without history, symptoms or neurological signs of brain pathology, or at the time of examination does not have severe alkalosis, anoxemia or hypoglycemia, or other metabolic disorders associated with dysrhythmia, his disordered potentials are doubtless genetic in origin.

On the basis of present knowledge, the electroencephalogram does not give precise information as to whether a person with only moderate increase or decrease of the dominant frequency carries a predisposition to epilepsy, or to any nervous disorder associated with a high incidence of dysrhythmia. The eugenic significance of genetic dysrhythmia deserves thorough long term study.

The undesirable trait of a tendency to seizures may be outweighed by the presence in the epileptic and in the spouse of physical, mental or spiritual traits which are highly desirable. Answer to the question of marriage and children is individual and not general. Some epileptics should and some should not marry.  
2 figures.

## PREMATURE DELIVERY, CAUSES AND RESULTS

ETHEL S. DANA

Am. J. Obst. & Gynec., 51: 329-342, 1946

The credit for the decrease in mortality in premature infants in recent years belongs, in most part, to the pediatrician. However, the responsibility for the prevention of premature delivery and for the delivery of premature infants in the best possible condition rests upon the obstetrician. It is therefore interesting to study the causes and results of premature delivery.

The author has studied a series of 941 cases of premature delivery. Regardless of the duration of pregnancy, the infant was considered premature if its birth weight was between 1500 and 2499 grams, or if its length was between 35 and 44.9 centimeters. The incidence of prematurity in this clinic was found to be

2.95 per cent. In this series it was not indicated that sterility is related to premature labor.

The causes for the onset of premature labor may be considered as maternal, fetal or placental. In 20.0 per cent of this series, premature delivery was the result of induced labor and these cases are not included in the statistics dealing with spontaneous premature labor. Table II shows the incidence of the various factors among the causes of premature delivery.

TABLE II  
*Causes of premature delivery*

	INCIDENCE IN PREMATURE GROUP; NO OTHER FACTOR	INCIDENCE OF CONDITION	
		Premature group total	Total clinic
Maternal			
Toxemia, all types.....	8.5	21.7	7.3
Syphilis.....	0.5	1.9	1.7
Pulmonary disease.....	1.0	1.4	—
Pyelitis.....	0.6	1.2	—
Pelvic pathology			
Myoma uteri.....	2.1	3.4	1.3
Bicornuate uterus.....	0.5	0.7	—
Ovarian cyst.....	0.1	0.3	—
Previous pelvic surgery.....	2.0	7.7	4.8
Other.....	0.8	2.4	—
Cardiac disease.....	1.5	3.4	3.0
Fetal			
Deadborn macerated infant.....	3.9	10.1	0.5
Twins.....	5.3	7.7	1.2
Triplets.....	0.3	0.3	0.009
Congenital abnormality.....	2.8	4.2	0.5
Hydramnios.....	0.2	1.2	0.3
Placental			
Placenta previa.....	0.6	3.8	0.5
Premature separation.....	1.8	4.3	0.4
Premature rupture of the membranes.....	16.8	33.7	24.5

It may be concluded that although toxemias are a major cause of prematurity, they are so chiefly because of their associated high incidence of artificial delivery before term, intrauterine fetal death, premature separation of the placenta, hydramnios and twins. Toxemias per se account for a definite but relatively small percentage (8.5 per cent) of premature labors. Where syphilis was found, adequate therapy was promptly administered in most of these cases. All of the cases having pulmonary complications had acute febrile reactions which might account for the premature labor.

Among the fetal causes it may be seen that all of the conditions are much more frequent in premature infants than in the whole clinic. The cases of deadborn macerated fetuses are interesting in that 37 cases had no other complication

present and the cause of death was unknown in all but 6. The toxemias of pregnancy were associated with 30.7 per cent of the deadborn macerated group. The cases of multiple pregnancy are also associated with a large incidence of toxemia.

In respect to placental causes of premature labor, it is noted that the chief role of placenta previa is that of forcing the hand of the obstetrician rather than actually precipitating labor. Also, it is of interest that one-quarter of the cases of premature separation of the placenta were associated with the toxemias of pregnancy. With the exception of these 2 important factors, it is difficult to evaluate the role of the placenta. The number of infarcts in the placentae of

TABLE X  
*Obstetric factors in fetal mortality*

	NUMBER OF CASES	INCIDENCE		
		Gross fetal mortality	Corrected fetal mortality	Survival rate
Duration of labor (cesarean sections excluded)				
Precipitate.....	101	29.7	14.9	70.3
Average.....	813	32.7	17.7	67.3
Prolonged.....	42	33.3	16.7	66.7
Type of delivery				
Spontaneous.....	729	29.1	15.3	70.7
Low forceps.....	54	26.0	16.7	74.0
Midforceps.....	5	20.0	20.0	80.0
Breech extraction.....	135	46.3	31.6	53.7
Version and extraction.....	24	58.3	20.8	41.7
Cesarean section.....	71	47.0	29.4	53.0
Perineum (spontaneous deliveries only)				
Episiotomy.....	189	14.8	12.2	85.2
Intact.....	389	33.4	16.2	66.6
Laceration.....	100	29.0	17.0	71.0
Analgesia				
Morphine.....	200	39.5	23.0	60.5
Other.....	143	32.2	18.2	71.3

patients with toxemias was increased. It is suggested that premature rupture of the membranes, in some cases at least, is a precipitating factor of premature labor rather than merely an incident in its course.

In those patients in whom there was no apparent cause for premature labor, it was noted that the infants were born closer to term and were somewhat heavier than the average premature in this series. It is suggested that a number of these infants, classified as premature, are actually full-term infants who have failed to attain the weight of 2500 grams.

The obstetric management and complications at the time of delivery have an important bearing on the end results of premature delivery. It is not surprising

to find an increase in breech and other abnormal presentations in infants delivered before term since breech presentation is well known to be more frequent in the antenatal period.

In this clinic, it is felt that a spontaneous delivery, with a deep episiotomy, is the procedure of choice for a premature infant. For this reason, and because of the relatively short 2nd stage in premature labors, there was a low incidence of forceps deliveries in this series. The incidence of operative delivery was 27.9 per cent. Cesarean section was performed more than twice as frequently as in the general clinic; two-thirds of these sections were performed because of placenta previa, premature separation of the placenta or toxemia of pregnancy. It is generally believed that analgesic agents should be used sparingly in premature labors. Morphine is contraindicated.

The gross infant mortality in this series was 33.3 per cent. This includes all deadborn and stillborn infants and those who died during the neonatal period. The corrected infant mortality, which was 18.8 per cent, excludes all deadborn macerated fetuses and those with congenital abnormalities incompatible with life. The most important factor in the mortality of premature infants is the birth weight. The value of various obstetric procedures may be judged from Table X.

The maternal morbidity rate was 15.7 per cent and puerperal infection was present in 10.4 per cent. In the general clinic the corresponding rates were 9.4 per cent and 7.2 per cent, respectively. This increase may be partly due to the large number of operative deliveries.

It is concluded that the causes of premature delivery are, in many cases, beyond the control of the obstetrician. His role in the prevention of prematurity consists in the control of syphilis and febrile diseases, and in continued research on the toxemias of pregnancy.

The availability of prompt oxygen therapy and expert pediatric care is of prime importance to the premature infant.

## ASPHYXIA OF THE NEWBORN INFANT

J. D. RUSS AND R. A. STRONG

*Am. J. Obst. & Gynec.*, 51: 643-651, 1946

The acquisition of the knowledge necessary to safeguard all newborn babies from asphyxia and treat them if it occurs, is an obligation which must be assumed by everyone who accepts the responsibility for the care of the newborn. Anoxemia, from many causes, is responsible for 18.5 per cent of all deaths in newborn babies and is fourth in the causes of death in this age group.

Most frequently the causes of asphyxia are found in the mother and in the handling of the mother during labor. After the age of 35, mothers are more

likely to deliver an asphyxiated baby than they are prior to this age. In general, primiparae produce more asphyxiated babies than do multiparae. Cyanosis is quite liable to occur when the mother is profoundly anemic.

By far the most outstanding single cause of asphyxia of the newborn is prolongation of labor. The more traumatic the type of delivery, the higher the death rate and asphyxia rate. It is the authors' belief that, if a routine intratracheal catheterization of the newborn be done at every cesarean section immediately upon delivery, the death rate in this type of delivery could be reduced from an average of 8 to 10 per cent to as low as 2 per cent.

Observations by the authors seem to justify the assertion that the use of pentobarbital sodium should be discontinued and that morphine should not be administered if delivery is possible within 4 hours. Greater reliance should be placed on the relatively harmless barbiturates. Among the anesthetics, ether has little or no effect on the baby that cannot be overcome rather easily. Chloroform and cyclopropane should be given only by experienced anesthetists.

Other less frequent causes of asphyxia are prematurity, premature separation of the placenta, bleeding placenta previa, short cord, and prolapse, torsion, knot, kink or compression of the cord.

Anoxemia prolonged for more than 2 minutes after delivery will cause serious cerebral changes. However, the prompt initiation and maintenance of respiration within 30 seconds after cutting the cord will prevent these changes, and if it is established before 2 minutes it may oxygenate the blood sufficiently to arrest any changes which have begun. In order to achieve good resuscitation, the following 4 principles must be followed: (1) a minimum of handling; (2) immediate warmth; (3) a clear open airway; and (4) oxygenation of the blood stream within 30 seconds of severing the cord. The latter should not be severed until it has ceased to pulsate. Aftercare of the newborn resuscitated baby is of equal importance.

The results of the study of 1048 additional cases of asphyxia to 196 previously reported have been analyzed and tabulated.

## INTRAUTERINE FOETAL DEATH DUE TO RHESUS INCOMPATIBILITY

LOUIS RESNICK

J. Obst. & Gynaec. Brit. Emp., 53: 62-67, 1946

The object of this paper is to present data collected from the literature which may simplify the diagnosis of intrauterine fetal death due to Rhesus incompatibility, and assist in the management of such cases during and after pregnancy, thereby lessening the hazards of incompatible blood transfusions and their attendant dangers.

**Diagnosis:** A detailed history of previous pregnancies is important, especially in multiparae who have had one or more infants developing jaundice or pallor soon after birth, which children have died without or recovered with a transfusion. One or more unexplained stillbirths, premature labors or neonatal deaths should be suspected as being due to hemolytic disease until disproved.

According to Henderson, in the variation of erythroblastosis fetalis which is characterized by fetal maceration, hydramnios is common. In the majority of cases with hydrops, uterine enlargement is out of all proportion to the duration of the amenorrhea.

The finding in the mother's blood of typical agglutinins (usually anti-Rh) can be accepted as almost conclusive evidence of affection. However, failure to find the agglutinins, say 20 days after delivery, does not exclude the diagnosis. The finding of antibody during pregnancy does not prove that the fetus will necessarily suffer from erythroblastosis, firstly because the fetus may be Rh negative (if the father is heterozygous) and therefore not affected, and secondly because on rare occasions it has been shown that an Rh negative mother with Rh antibody during the puerperium may have an Rh positive baby which does not show signs of the disease.

The possibility of excessive infarction of the placenta due to syphilis with intrauterine fetal death and the birth of a macerated infant is generally accepted as one of the commonest causes of late abortion. A routine prenatal Wassermann reaction will usually establish the diagnosis, although concomitant Rh incompatibility cannot be excluded.

On x-ray examination, the frog-like attitude of the fetus *in utero* is an important diagnostic feature of fetal hydrops, which is further characterized by a halo around the fetal head due to edema of the scalp. Overlapping of the fetal skull is a well known sign of maceration and fetal death.

In cases of hydrops, autopsy findings usually reveal a grossly edematous fetus. The liver and spleen show some degree of degeneration, pigment deposits and hemopoiesis. In cases of maceration the fetus shows little or no edema, marked maceration and diffuse hepatic cirrhosis and splenomegaly. The placenta is almost always edematous and pale pink in color with microscopic changes of fibrosis, edema and hemopoiesis.

Other conditions causing intrauterine fetal death before term are syphilis, chronic nephritis, essential hypertension, diabetes mellitus, ? excessive calcification of the placenta, abnormal carbohydrate metabolism and other unknown causes.

**Management:** The chief aim would be to obtain a normal delivery, prevent complications in the 3rd stage of labor and prepare for the immediate treatment of excessive bleeding, should it occur. The necessity for Rh negative blood is stressed; a suitable donor should be made available. In the absence of suitable blood, in cases of emergency, it is suggested that plasma be administered until Rh negative blood is available.

The suggestion of routine Rhesus investigation in all pregnant women is supported, in order to avoid transfusion reactions. The avoidance of further

pregnancies, following several unsuccessful pregnancies due to Rhesus incompatibility, is advisable.

## THROMBOCYTOPENIC PURPURA IN PREGNANCY AND IN THE NEWBORN

WILLIAM B. PATTERSON

J. A. M. A., 130: 700-702, 1946

According to Polowe, 62 cases of pregnancy complicated by thrombocytopenic purpura have been recorded in the literature. The mortality was about 55 per cent for the mothers and was slightly higher for the infants. The maternal mortality was usually due to uterine bleeding after delivery and some of the infants are reported to have died of hemorrhage; part of these were known to have thrombocytopenia. It is suggested that congenital thrombocytopenic purpura may occur.

The patient who is the subject of the case report presented in this paper was known to have had chronic purpura and thrombocytopenia since the age of 4. She became pregnant against medical advice but pregnancy and labor were normal. A smooth blade obstetric forceps was used to complete delivery. After spontaneous delivery of an intact placenta no tears of the cervix, vaginal walls, labia or perineum were noted. Fifteen minutes after delivery of the placenta a very slight amount of vaginal bleeding was noted, although the uterine fundus was very firm. About an hour later the vagina was found to be filled with a large clot which, when removed, was seen to have been attached to a rend in the vaginal wall at the exact location at which the obstetric forceps blade had contacted the tissue. The bleeding was controlled by uterine and vaginal packing and glucose infusion and blood transfusions were given. The patient was discharged on the 11th postpartum day. At that time the involution of the pelvic organs was progressing normally and the tear in the vaginal wall had healed.

The infant was a normal boy. Sixty hours after birth it was noted that a faint forceps mark on the right cheek which had almost disappeared had suddenly become dark blue. A purpuric spot was also noted on the right forearm. Seventy-two hours after birth there was blood with the normal stool. The bleeding time was 4 minutes and the platelet count was 18,570. Transfusions were given, after which each succeeding stool contained less blood and the purpuric lesions gradually disappeared. On the 75th day of life the child had had no purpuric spots since leaving the hospital. The bleeding time had decreased to  $\frac{1}{2}$  minute and the platelet count had risen to 175,000.

To recognize thrombocytopenic purpura in pregnancy before an acute attack and before delivery, one must suspect it in all patients who have shown any

abnormal bleeding, who have close relatives who are "bleeders", or who have had postpartum hemorrhage at previous deliveries. The treatment in acute hemorrhagic purpura is multiple small transfusions. Splenectomy may be necessary, but only as a life-saving measure when conservative measures have failed.

Every pregnant purpuric patient should be hospitalized at the onset of labor. Immediately after delivery of the placenta the uterus and vagina should be packed firmly. Almost all the deaths have occurred from slow continuous bleeding in the days following delivery. All infants of mothers with thrombocytopenia should be blood typed and a bleeding time and platelet count should be made. The treatment for the infant with hemorrhagic purpura is also repeated small transfusions.

It is concluded that pregnancy is far too dangerous an undertaking for a woman who has chronic thrombocytopenic purpura. The danger can be enhanced by the development of late toxemia, since placentas of patients with late toxemia usually contain many infarcts.

## THE FETAL MORTALITY IN WOMEN DURING THE PREDIABETIC PERIOD

JOSEPH HERZSTEIN AND HENRY DOLGER

*Am. J. Obst. & Gynec.*, 51: 420-422, 1946

The fact that Miller, Hurwitz and Kuder reported an unusually high fetal and neonatal mortality rate even 20 years before the onset of maternal diabetes prompted the authors to analyze the prediabetic fetal and neonatal mortality among a group of diabetic mothers.

The data presented in this study were obtained from 200 married diabetic mothers. Eighty-three per cent of these women had children before the age of 31. Although the onset of diabetes developed at a mean age of 45.7 years, almost half of the patients first noted diabetes before the 45th year.

The total infant fatality rate (stillbirths and deaths within 10 days after birth) was 6.1 per cent. The corresponding rate for nondiabetic women as given by others ranged from 2 to 6 per cent.

The fetal fatality rate for the first 5 years preceding the onset of recognized diabetes was 15.4 per cent. The first 5-year prediabetic period revealed an increased fetal and neonatal mortality but the preceding 15 years were not characterized by such a tendency. The total rate for the entire 20-year prediabetic period did not differ significantly from normal. The rate for the total 20-year prediabetic period was about the same as that for the period of over 20 years, namely, 6 per cent.

The stillbirth and neonatal fatality rate among women who were destined to have diabetes severe enough to require insulin was not higher than among those who developed mild diabetes.

On the basis of 714 pregnancies among the 200 women, the spontaneous abortion rate was 12.3 per cent. The corresponding figure for the general population reported by White was 11 per cent for "miscarriages or abortions."

## CONGENITAL SYPHILIS; REPORT OF POSSIBLE THIRD GENERATION SYPHILIS WITH FATAL SPONTANEOUS CEREBRAL HEMORRHAGE

LAURENCE J. UNDERWOOD

*Am. J. Syph., Gonorr. & Ven. Dis.*, 30: 54-57, 1946

The author presents the case of a 5 year old boy who was referred by an oculist with typical manifestations of acute interstitial keratitis. The remainder of the physical examination revealed questionably confirmatory evidence of late congenital syphilis. Neurologic findings were entirely normal. Repeated blood Kahn and Kolmer serologic tests were strongly positive before and after institution of treatment. Past history revealed no other manifestations of early congenital or acquired syphilis.

The eye signs and symptoms responded well to treatment which consisted of a preliminary course of mapharsen and thiobismol and 7 malarial paroxysms, totaling 68 hours of fever over 103° F. Following malaria, alternating courses of weekly mapharsen and bismuth subsalicylate were given. About 7 months after the beginning of treatment, the patient unexpectedly died from massive cerebral hemorrhage from the rupture of a cerebral vascular anomaly.

Investigation of the mother has revealed no history of early or late syphilitic manifestations. No known syphilis existed in her first husband and her present husband has had repeated negative clinical and blood serologic tests. The mother had a prenatal negative Kline diagnostic serologic test and denies extramarital sexual contact. Physical examination of the child's mother revealed no evidence of acquired or congenital syphilis and serologic tests with standard and quantitative Kahn, Kolmer and Kline methods have been reported entirely negative from 4 different laboratories over a 12 month period.

Examination of the maternal grandmother, aged 69, disclosed no confirmatory signs of visceral, neurologic, cardiovascular or other late manifestations of syphilis. Standard Kahn and Kolmer and quantitative Kolmer blood serologic tests have been strongly positive in 3 laboratories. There is no history of early syphilis, treatment or previous knowledge of infection.

It is believed that this child had active syphilitic interstitial keratitis which is almost always a manifestation of congenital syphilis. Third generation syphilis with serologic and clinical latency in the second generation should be considered a possibility. The criteria of Fournier and Finger in suspected cases are: (1) acquired syphilis must be demonstrated in the grandmother and prefer-

ably also in the grandfather; (2) parental as distinguished from acquired syphilis must be demonstrated in the mother of the third generation case, and the father must be proved healthy; (3) there must be incontestable evidence of third generation syphilis; (4) manifestations must appear soon after birth in both the second and third generation.

It is suggested that a possibility of second and third generation syphilis existed in this case, although the criteria of Fournier and Finger cannot be completely fulfilled.

## THE EFFECTS OF OXYGEN ON THE CIRCULATORY SYSTEM IN CONDITIONS OF ANOXIA AND ASPHYXIA

GEORGE W. STAVRAKY

Canad. J. Research, 23: 175-194, 1945

The author presents an analysis of the blood pressure changes during anoxia, asphyxia and oxygen administration in 34 animal experiments. Similarly, in 30 human subjects during decompression equivalent to altitudes ranging from 16,500 feet to 29,000 feet, the blood pressure findings are correlated with the action of the heart and the state of the peripheral blood vessels, and the effect of the subsequent administration of oxygen upon them is investigated.

Sudden deprivation of oxygen leads to a vasoconstrictor response which, in humans, manifests itself in facial pallor and elevation of blood pressure. The administration of oxygen in the later stages of this response may produce a further transient elevation of the blood pressure, which is followed by a fall of blood pressure and decrease in pulse rate. The rise of blood pressure caused by oxygen after a period of acute anoxia or asphyxia is due to an augmentation of the action of the heart and to an intensification of vascular tone, the 2 phenomena contributing to the rise of blood pressure in varying degree under different experimental conditions. In intact, anesthetized cats the effect persists after adrenalectomy. In spinal preparations, previously kept on "minimal" respiration, the effect is greatly reduced by the removal of the suprarenal glands. The rise in blood pressure resulting from the administration of oxygen is abolished by the destruction of the spinal cord by pithing, and is therefore attributed to an excitation of the sympathetic centers. Evidence also is presented that suggests that the chemoreceptors participate in this response in intact anesthetized animals.

A protracted oxygen deficiency of a moderate degree leads to a vasodilator reaction. In human subjects it manifests itself in a gradual engorgement of the cutaneous blood vessels, often in a lowering of the blood pressure and an increase in the pulse rate. Sudden administration of excessive quantities of oxygen under these conditions causes a further decline of blood pressure and a slowing

of the pulse. An analysis of the fall of blood pressure caused by the administration of oxygen in conditions of prolonged hypo-oxygenation shows that it is not strictly related to changes in respiration or to acapnia, which occurs during breathing of air deficient in oxygen. Neither is it prevented by addition of carbon dioxide to the oxygen. However, under prevailing experimental conditions this fall of blood pressure is almost invariably abolished by a bilateral vagotomy, is occasionally reduced by atropine, and is absent in spinal preparations, these observations indicating that it is dependent on the functioning of the medullary reflex mechanisms.

## OPERATIVE OBSTETRICS

### A PARAVESICAL EXTRAPERITONEAL CESAREAN SECTION TECHNIQUE; WITH AN ANALYSIS OF 160 PARAVESICAL EXTRAPERITONEAL CESAREAN SECTIONS

JAMES FRANCIS NORTON

*Am. J. Obst. & Gynec.*, 51: 519-526, 1946

There still occur obstetric problems which can best be handled by recourse to an extraperitoneal cesarean section. The author presents, in this paper, a paravesical extraperitoneal cesarean section technique which has served very well at the Margaret Hague Maternity Hospital, with an analysis of 160 paravesical extraperitoneal cesarean sections performed with various techniques.

The average duration of labor for the entire group was 42.6 hours, and the average duration of labor with membranes ruptured was 29.8 hours. The intrapartum morbidity rate was 6.7 per cent. The peritoneal cavity was opened 44 times, or in 27.5 per cent of the total. Nine, or 5 per cent of the total, had the bladder injured; 8 of these occurred in the first 63 cases. The postoperative morbidity in the entire group was 98, or 61.2 per cent. There were 3 maternal deaths; one in 1935 from infection, another in 1936 from infection and one in 1938 from hemorrhage.

There were 9, or 5.6 per cent, stillbirths or neonatal deaths. Thirty-nine, or 24.4 per cent, of the infants born weighed 3800 grams or more.

There were 116 cases with an intact peritoneal cavity and of these 59 per cent had a morbid postoperative course. This is compared with 66 per cent of those morbid with the peritoneal cavity opened.

The author presents a step-by-step description of a particular paravesical extraperitoneal cesarean section technique, with illustrative line drawings. Speaking specifically and directly of this technique, it is claimed:

1. Relatively easy access is gained to the retrovesical area of the lower uterine segment.

2. Identity of the posterior peritoneal fold is thus possible.

3. This retrovesical area can be enlarged under direct vision infraperitoneally.

4. Sufficient room is obtained to deliver baby of more than average size.

5. In the use of this technique there was no injury to any ureter or to any large vessel at the site of the uterus; the ureter was never within the field of operation. There was no extension of the incision into the broad ligament on either side; no massive infection of pelvic cellular tissue occurred. There were no injuries to the bladder in the vesicovaginal area; there were no permanent vesicovaginal fistulas; there were no maternal deaths.

6. Adequate exposure for either a vertical or transverse incision in the uterus is obtained.

7. The operation is well within the capacity of any competent obstetric surgeon. 3 figures.

## THE OBSTETRICAL FORCEPS: CONTROLLED AXIS TRACTION

JAMES BAXTER

*J. Obst. & Gynaec. Brit. Emp.*, 53: 42-54, 1946

With experience of controlled traction it seems possible to acquire a knowledge of the limits to which the traction force can safely be raised in the forceps operation.

The author presents with illustrations a method of controlling axis-traction. The traction force is determined wholly by the resistance of descent of the head; the greater the resistance the greater the pull, and with the forceps applied to the sides of the fully flexed head, the force compressing the fetal skull will bear a more or less constant relation to the traction force. Thus it is possible to demonstrate a definite relation between the traction force and the force compressing the fetal head and to arrive at an approximation of the maximal force which can be exerted on the forceps with safety to mother and infant and beyond which stillbirth and severe maternal lacerations would seem inevitable. This statement is qualified by the following requirements.

(1) That the fetus be an average full-time one weighing between 7 and 8 pounds.

(2) That the head be fully flexed and the long diameter brought antero-posteriorly.

(3) That the forceps be applied to the sides of the head.

Evidence is presented to suggest that the fetal brain can withstand only a small amount of compression force. The fetal skull responds to the compression force by altering its shape but, when the limits of this alteration are reached, the force is communicated to the brain itself and here the impact of a force equivalent to something less than the tensile strength of the falx is apparently sufficient to cause fetal death. The evidence suggests that death is produced by comparatively small compression forces reaching the brain and that gross lesions are the results of these forces continuing to rise after death.

Experimentally it was found that when traction is made on the forceps intracranial pressure begins to rise very early and fairly regularly up to a traction force of 50 pounds. From 50 pounds up to 70 pounds the rise of this pressure is more rapid. A force of 70 pounds appears to be, in the fetus weighing from 7 to 8 pounds, a critical level of traction since in most cases it has been impossible to obtain any rise in intracranial pressure when the force is raised beyond this. The water level remains stationary even when the force has been raised to 100 pounds and the inference is drawn that traction at about 70 pounds compresses the cranial contents to the extent of interfering with the movement of cerebro-

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spinal fluid from the cerebral system to the spinal canal. The earlier signs of severe compression in the extremely moulded head and their delayed appearance in the unmoulded head are exactly what would be expected.

In practice most operations are completed with a force no greater than 50 pounds. The need for greater force suggests the presence of some abnormality such as the following:

- (1) Malposition of the head.
- (2) Extension of the head.
- (3) Disproportion between head and pelvis.
- (4) Other obstruction.
- (5) Malposition of the forceps.
- (6) Large fetus.
- (7) Too early application of forceps.

The author suggests a method of forceps extraction. 8 figures.

## MISCELLANEOUS

### A REVIEW OF THE MATERNAL MORTALITY AT THE CHICAGO LYING-IN HOSPITAL, 1931-1945

M. E. DAVIS AND T. G. GREADY, JR.

Am. J. Obst. & Gynec., 51: 492-513, 1946

The maternal mortality at the Chicago Lying-In-Hospital has decreased steadily during the last 13 and one-half years and the curve parallels the national curve. The most rapid decline has occurred in the last 4 years. There were 81 deaths in 47,945 obstetric patients, an over-all mortality of 0.17 per cent of all pregnant patients.

Sixty-four of these patients were delivered and died in the hospital; 11 were delivered in their homes and were sent to the hospital in the postpartum period; 3 were delivered and died in their homes; 2 were delivered in the hospital but died at home within the first 8 weeks after delivery; one patient was sent to another hospital by the Home Service and died there.

The youngest patient was 19 and the oldest 43 years of age. The average age of the group was 29.4 years. A recent report by Eastman once more emphasizes the increased hazards of childbirth late in the reproductive career.

In 53 patients the duration of pregnancy was longer than 36 weeks; in 11 from 30 to 36 weeks; in 9 from 20 to 29 weeks; and 8 women were less than 20 weeks pregnant.

In general, the authors' mortality figures, in respect to the causes of death, follow the general pattern. Infection was the principal cause of death, accounting for 39.5 per cent of the total, while the corresponding national figure was 38 per cent for the year 1941. Hemorrhage and shock contributed 16 per cent, whereas the toxemias of pregnancy contributed 7.4 per cent. These compare with 26 and 25 per cent for the country at large. Heart disease accounted for 16 per cent of the deaths. Autopsies were performed in 77 per cent of the 81 patients who died. Preventable factors were present in 2 out of every 3 deaths.

The authors summarize the management of the complications responsible for mortality at their institution:

*Infection.*—If the statistics of this hospital are an example of the trend in large institutions, infection is rapidly disappearing as a major cause of death in obstetrics. This can be ascribed first to the introduction of the sulfonamides and penicillin. The institution of duodenal drainage and decompression of the distended abdomen have decreased the hazard of peritonitis. The liberal use of blood, plasma and parenteral fluids has provided efficient tools for the treatment of infection. Lastly, better obstetrics has decreased the hazards of infection. Of the 32 deaths (39.5 per cent) due to infection in this series, the infection was genital in origin in 19 instances and extragenital in 13. All the deaths from

puerperal infection occurred prior to July 1, 1939, and since that time almost 20,000 women have been delivered without a single death due to this cause.

*Hemorrhage.*—In 13 cases in this clinic hemorrhage was the primary cause of death, and it was a contributory factor in many other fatalities. Three women died as a result of incompatible blood transfusion and would otherwise be alive. It is noted that an excessive loss of blood influenced directly or indirectly the clinical course of almost one-half of these women who lost their lives in childbirth.

Hemorrhage and its resultant shock is a preventable complication in many cases, and is amenable to adequate therapy in most cases. Management includes the proper treatment of the etiologic causes. Two deaths in this series were charged to placenta previa and both deaths were considered preventable by present standards. Early recognition of the presence of abnormal placental implantation is essential. In incomplete placenta previa delivery from below is favored, with rupture of the membranes or, if this fails to control bleeding, Willet's method of scalp traction adds no great hazard. The use of Braxton-Hicks' version and insertion of a bag have no real place in the management of this complication. Patients with complete placenta previa are best treated by cesarean section and delay in operation may increase the likelihood of infection.

Abruptio placentae was the cause of 2 deaths; in both instances delivery was accomplished vaginally and one of the deaths was considered preventable. The mild cases of abruptio placentae can be treated conservatively. The patient who presents a picture of massive hemorrhage is better treated by cesarean section. If, after emptying its cavity, the uterus fails to contract, hysterectomy should follow.

Postpartum hemorrhage accounted for at least 4 of the 13 deaths and all 4 were considered preventable in the light of present knowledge. The most common cause of excessive blood loss in the third stage is the mismanagement of this important period. Trauma is also a major cause of postpartum bleeding.

The liberal use of blood, plasma and parenteral fluids is important in all of these hemorrhagic conditions.

*Uterine rupture.*—Seven women with rupture of the uterus died. In 4 of these patients the rupture occurred following version and extraction and the authors present several well known suggestions to increase the safety of this procedure when it is indicated.

*Heart disease.*—Unlike the national maternal mortality statistics, heart disease shares second place with hemorrhage as one of the 3 most important causes of maternal death, being the primary factor in 13 cases. In about 95 per cent of these cases in the obstetric services, the heart disease is rheumatic in origin. The authors describe the treatment of obstetric patients with heart disease. The important aspect of this problem is that the medical management of the cardiac patient is the most important phase of her obstetric care.

*Toxemia.*—The toxemias of pregnancy were directly responsible for 6 deaths, although 23 of the 81 patients who died had symptoms and findings of toxemia. Fatalities are largely preventable in the management of the toxemias of pregnancy and this management is outlined.

*Cesarean section.*—Eleven of the 81 women who died were delivered by the abdominal route. In at least 3 cases the operation was performed entirely in the interest of the baby and in 3 other patients inexperience of the surgeon was a major factor in the fatality. Cesarean section in the hands of the specialist need carry no great risk. The explanation for the existing mortality rates in cesarean section lies in the selection of patients for this procedure. The safest time to perform a cesarean section is before the patient goes into labor or after a carefully conducted test labor of less than 24 hours.

Anesthesia, embolism and transfusion reactions as causes of death are discussed. These 3 factors were responsible in this series for 2, 6 and 3 deaths, respectively. 3 figures.

(An excellent report of an excellent record.—Ed.)

## AN ANALYSIS OF THE OBSTETRIC ACTIVITIES IN HOSPITALS OF COOK COUNTY DURING 1944

CHARLES NEWBERGER

*Am. J. Obst. & Gynec.*, 51: 372-386, 1946

By means of tables, graphs and maps, the author presents a statistical analysis of the obstetric activities in hospitals of Cook County during 1944. The 3 main aspects of the study are mothers, infants and mortality.

It is shown that of the 69,079 mothers cared for, 70.2 per cent had spontaneous deliveries; among the 29.8 per cent of those who had operative intervention for the birth of the infant, there were 24.3 per cent forceps cases, 3.6 per cent cesarean sections, 1.5 per cent breech extractions, 0.3 per cent version and extractions, and 0.1 per cent craniotomies.

In addition to these 29.8 per cent receiving aid in delivery, another 3.7 per cent of the mothers required operative procedures for other purposes, such as mechanical induction of labor in 0.3 per cent, manual removal of the placenta in 0.5 per cent, uterine packing in 0.4 per cent, and transfusion in 2.5 per cent. Disregarding the very small number of women who may have had more than one operative procedure, it is noted that one-third of all mothers had some type of intervention during the birth process.

Of all mothers whose pregnancies ended at term or prematurely, 9.5 per cent had some form of obstetric complication: 4.4 per cent had infection, 2.9 per cent had toxemia, and 2.2 per cent had hemorrhage. Another 0.1 per cent had non-obstetric complications involving the various organs of the body. In addition to these mothers, 9.6 per cent of all who were delivered, there were recorded 2,298 other women as obstetric casualties; 2103 who aborted and 195 who required surgical treatment for ectopic gestation.

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# Maternal Mortality Reports

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*(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.)*

*Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)*

## CASE NO. 16

The patient was a colored, 39 year old para 9 with a negative Wassermann and a normal pelvis. The expected date of confinement was the third week in May. She was admitted to the hospital on March 15th because of painless vaginal bleeding. Sterile vaginal examination did not reveal placenta previa and the bleeding was attributed to a friable eroded cervix. The patient was discharged a day later.

Intermittent bleeding continued and she was readmitted because of this on April 8th. P.E.: Small fetus in R.O.T., with floating head. F.H. in R.L.Q. Vaginal examination, done under anesthesia, 9:15 P.M., April 8th. Cervix was dilated sufficiently to admit two fingers, with the canal partly obliterated. Membranes intact. Internal os completely covered by placenta, which extended two inches to right of internal os. The membranes were ruptured and Braxton-Hicks version performed. During this procedure the cervix was torn so that the os approached full dilatation, and therefore the breech descended through the cervix. With very slight traction the infant was delivered. The child weighed 1950 grams and showed clinical evidence of intracranial damage. It died 24 hours later. Autopsy showed prematurity but no lesions.

Following delivery there was severe hemorrhage which lessened somewhat after manual removal of the placenta. The bleeding, however, was sufficiently severe to warrant immediate examination of the cervix and uterus. A cervical tear, thought to extend nearly to the lower uterine segment, was palpable on the left. No rupture of the fundus was felt. Since the tear was so high and the vagina so deep, it was impossible to visualize the point of bleeding. Therefore, tamponade of the uterus and vagina was carried out with Holmes' packer. Blood loss was estimated to be 800 cc. The patient remained in reasonably good condition, with a blood pressure of 110/60; pulse 150. She was given 500 cc. of 5 per cent glucose and 16 mg. of morphine and sent to her bed.

Thirteen hours later the patient was returned to the operating room to remove the pack. Her temperature was now 99.4 degrees; pulse 120; blood pressure 110/70. The pack was removed and 5 minutes later bleeding recommenced. As the uterus was tightly contracted and the top of the cervical tear could not be exposed, it was decided to repack the vagina with gauze. This controlled the bleeding after an estimated loss of 300 cc. Following this the patient went into profound shock. Intravenous glucose and transfusion were given. A second transfusion was given the same afternoon and the patient seemed temporarily improved. The following morning, however, the pulse had become very rapid (160) and the blood pressure was 102/62. Serosanguineous ooze from the pack. Twenty-four hours after the second pack had been inserted the temperature rose to 103.2 degrees; hemoglobin 62; patient delirious. Sulfanilamide was started. Thirty-six hours after insertion of the second pack, the hemoglobin had dropped to 25 per cent. The patient was transfused and the pack slowly removed. The blood culture which had been taken 24 hours after insertion of the second pack grew out *B. welchii*. The patient became oliguric; because of this she

Of the 69,823 infants delivered, 98.0 per cent were born alive, 3.9 per cent were premature births, and 0.3 per cent were injured during the birth episode.

In noting the mortality on the basis of each 1000 births, there were 20.4 stillbirths, 20.1 neonatal deaths, and 1.7 maternal losses. Of the 119 maternal deaths in Cook County during 1944, puerperal infection ranked first in cause with 23.5 per cent, toxemia was second with 17.6 per cent and hemorrhage was third with 12.6 per cent; abortion with or without sepsis accounted for 21.9 per cent of all deaths, ectopic gestation for 7.6 per cent and a variety of other diseases for 16.8 per cent.

It is believed that critical examination by the profession of the information presented, and in particular, the study of each hospital staff of the report sent by the Division of Maternal and Child Hygiene of its own obstetric work, with comparative data for its birth class and for the State, should lead to improvement in trends of obstetric practice, to lowering unduly high operative rates in some institutions, to less frequent resort to cesarean sections in others, to more ready use of blood or plasma for prophylaxis or for treatment, and to the general leveling off of the peaks, and extremes, and marked variations in procedures. The consequence of such changes should reflect itself in a further reduction of mortality rates, making childbirth safer for the mother and her newborn infant.

Three months postpartum she was admitted to the medical department of the hospital with definite decompensation. After ten days' rest in bed and a return of compensation, the patient left the hospital against advice. Attempts to get her into local convalescent homes were unsuccessful.

A year and a half later the patient returned to the Obstetrical Service four months' pregnant. There was no frank decompensation at this time, but clear-cut evidence of a very low cardiac reserve. It was determined to do a vaginal hysterotomy, since the pregnancy was beyond the usual dilatation and curettage stage. Furthermore, it was planned to sterilize the patient by laparotomy later, when she was in better cardiac condition. Under open ether, vaginal hysterotomy was done, with about a 500 cc. blood loss. During the operation the pulse became thready, rising to 160 per minute. The patient became pale and clammy, with a drop in blood pressure. Pituitrin, caffeine, adrenalin, glucose and digifolin were all given during 45 minutes. Her condition improved, but the next day she was vomiting, with an irregular pulse of 140. The temperature was mildly elevated. On the fourth day there was dyspnea, with edema of the lungs and pinkish sputum. More digitalis and atropine were ordered; venesection was not done because of the low hemoglobin (48%). During the night of the fourth day the patient was placed in an oxygen tent, and despite more digifolin and morphine, she died.

Autopsy findings: Chronic rheumatic endocarditis of tricuspid and mitral valves; Mitral stenosis; Organizing rheumatic vegetations; Scars and Aschoff bodies in myocardium; Edema of lungs; Enlarged uterus, with infected placental fragments—organism gram-positive coccus (Beta strep.).

*Discussion:* The sequence *heart-failure-pregnancy* invariably carries a grave prognosis, particularly when the interlude between the two is less than 18 months as in this case. Accordingly, it was the opinion of the Committee that the primary circumstance responsible for this death was the patient's failure to avoid pregnancy, abetted by her delay in reporting for prenatal care until the fourth month. Had it been possible to perform therapeutic abortion at 8 or 10 weeks by simple dilatation and curettage, the patient might well have survived this less traumatic procedure.

Although this case was voted preventable on the grounds of faulty patient co-operation, the Committee thought it desirable to point out one major error in the management of the first delivery and to question the wisdom of the procedure used in terminating the second pregnancy. In the delivery of the first infant, forceps were applied "in order to avoid the strain of the second stage of labor." The result was a difficult mid-forceps extraction, which had to be preceded by a Scanzoni maneuver. Surely the "strain of the second stage" with this 1900 gram baby would have been minimal in contrast to the shocking trauma produced by this major operative procedure.—to which "the patient reacted badly." Thirty minutes of second stage pains (without bearing down) would not have hurt this patient and if gentle supra-fundic pressure had been used with each contraction, it seems highly probable that the head would have rotated spontaneously and come to the perineal floor within a half hour. Delivery could then have been effected with episiotomy and supra-fundic pressure or by episiotomy and easy outlet forceps. Mid-forceps have no place in obstetrics except when one's hand is forced by unyielding mechanical arrest; certainly, in the presence of heart disease, such a traumatic procedure should be avoided at all costs.

Just because vaginal hysterotomy is an extra-peritoneal procedure, it is as-

was given 50 per cent glucose, with no improvement. A fourth transfusion was given but during its administration the blood pressure suddenly rose to 150/100, with immediate vaginal hemorrhage. The patient died shortly thereafter.

**Autopsy:** Ruptured uterus; torn cervix. On left, cervical tear  $1\frac{1}{2}$  cm. long, and then a bridge of intact cervical tissue; above this 4 cm. longitudinal tear in lower uterine segment, giving rise to vaginal hemorrhage mentioned above, and extensive retro-peritoneal hemorrhage. Gangrenous endometritis. Acute splenic tumor. Transfusion reaction, kidneys. Dermoid cyst, right ovary. Small myomata of uterus, largest 5 cm. in diameter, on posterior wall of uterus, subserous in type. Pulmonary edema.

**Bacteriology:** Heart blood negative. Uterus: *Welchii*, *coli communior*; *Alpha strep.*; aerobic gram negative bacillus (not identified).

*Discussion:* The management of this case was characterized by lack of thoroughness in examination of the patient both before and after delivery and by bungling operative technique. The failure to make the diagnosis of placenta previa on the first vaginal examination was not a costly mistake apparently, and probably played no role in the ultimate fatal outcome, but it suggests either lack of thoroughness or inexperience on the part of the examiner. When the diagnosis of complete placenta previa was finally made on the second hospital admission, cesarean section should have been done immediately. It is a well established fact that central placenta previa is associated with such extreme vascularity and friability of the cervix that any method of delivery from below will be attended by extensive cervical laceration in a large proportion of cases. The course of this patient attests the truth of this statement most dramatically.

The primary error in this case was the performance of Braxton-Hicks version, an operation which has no place in the modern management of any type of placenta previa, let alone the central variety. But even after this error had been committed there was still a good chance to save the patient had the birth canal been explored. A hand should have been inserted into the uterine cavity, the lower segment rupture detected and immediate hysterectomy, accompanied by blood transfusion, performed. The inability to explore the tear suggests again either lack of thoroughness (an assistant is essential) or inexperience in operative obstetrics.

#### CASE NO. 17

The patient, an 18 year old white woman, had married at the age of 15, and became pregnant a year later. Early in that pregnancy she developed frequent attacks of dyspnea and precordial pain. Her family physician told her she had a "leaking" heart. She did not appear at the hospital until she was 34 weeks' pregnant, when the diagnosis of rheumatic endocarditis, with advanced mitral stenosis and insufficiency, and cardiac hypertrophy without decompensation, was made. After 5 days in bed in the hospital, the membranes ruptured spontaneously and after a 14 hour labor, the patient was delivered of a 1800 gram infant, which survived. Delivery was a rather difficult mid-forceps, with Scanlon's maneuver. The forceps was done as soon as the cervix was fully dilated, in order to avoid the strain of the second stage of labor. The patient reacted badly to the operative procedure, the pulse rising to 170 and becoming thready. She was given digitalis, post-delivery, and three weeks postpartum her teeth were extracted and tonsils removed. The patient was referred to the Contraceptive Clinic, but due to her desire for further children, this advice was not followed.

usual clinical findings and indeed, the main diagnostic features, of pelvic thrombophlebitis.

After considerable discussion the Committee voted this case a preventable death on the grounds that blood transfusions were not employed much earlier than they were. It will be noted that the chills and hectic temperature swings made their appearance on about the 7th day after delivery, that is September 28th, but that no blood transfusions were given until October 6th, some 8 days later. In the present state of our knowledge small blood transfusions, 200-250 cc., repeated every other day, are the most effective way of treating puerperal thrombophlebitis, regardless of the hemoglobin level, and might have saved this patient had they been given from September 29th onwards. This case occurred before penicillin was available. Today penicillin should be used in all such cases as it seems to be effective against many strains of the anaerobic streptococcus.

#### CASE NO. 19

The patient, a 19 year old, colored primigravida, whose expected date of confinement was June 12, was known to have a twin pregnancy. During the course of 7 prenatal visits no deviations from normal were detected, but at the 8th visit on May 28, the blood pressure was found to be 150/100, with a trace of albumin in the urine; there was only slight edema and no symptoms, but a weight gain of 4 pounds in a week was noted. The patient was admitted to the hospital at 11:00 A.M., May 28.

During the first 8 hours after admission the blood pressure rose to 190/110 and the albumin increased to 2 plus; meanwhile headache, vomiting and epigastric pain developed. Paraldehyde 20 cc., q. 4 hours per rectum was ordered.

Despite this therapy the blood pressure at 12 noon on May 29,—25 hours after admission—was 170/110 and the albumin 4 plus. The cervix barely admitted a finger tightly; the canal was recorded as almost 2 cm. long and the consistency firm. At 12:30 P.M. on May 29, the membranes were stripped back and ruptured artificially.

After a latent period of 3 hours, poor uterine contractions began followed by a first stage lasting 29 hours. The blood pressure remained at 170/110 with albumin 4 plus. Restlessness changed to apathy, then to semi-coma; anuria developed and the clinical picture resembled eclampsia without convulsions. At 6:00 P.M. on May 30—30 hours after induction—a generalized convulsion occurred.

Following the convulsion the blood pressure fell precipitously to 110/70; the pulse rose to 160 and the patient appeared to be in a state of collapse. She was still in semi-coma. After a 2½ hour second stage the patient was delivered without anesthesia of stillborn, macerated twins at 10:50 P.M., May 30,—about 34 hours after the induction.

Despite transfusion with whole blood the blood pressure continued to fall, marked edema of the lungs developed and the temperature rose to 104.3, pulse 170. Death occurred at 6:48 A.M., May 31, 8 hours postpartal. No autopsy.

*Discussion:* The death was considered by the Committee to be due to a two-fold error: (1) Induction of labor under circumstances which were utterly unfavorable for the procedure and (2) Failure to recognize the threat presented by fulminating pre-eclampsia in the presence of a twin pregnancy. It was the opinion of the Committee that it would have been much better judgment to have performed cesarean section at 12:30 P.M. on May 29, that is, at the time it was decided to rupture the membranes.

Right offhand it may be said that artificial rupture of the membranes to induce

sumed to be less shock-producing than abdominal hysterotomy. It should be noted that the patient lost 500 cc. of blood and one can be sure that forceful downward traction on the cervix was employed—because it is usually essential for good exposure in this operation. Would not abdominal hysterotomy under local anesthesia have been simpler and safer?—Less questionable is the criticism that the patient was not put into an oxygen tent until the night of the fourth day. She should have been put into one immediately after the operation.

#### CASE NO. 18

The patient, a 24 year old negress, had had two previous pregnancies which had been normal in every way, except that the first had resulted in the birth of living twins. With the present pregnancy nothing abnormal was made out except for a positive Wassermann. The syphilis was treated with a standard neo-arphenamine bismuth regime. The expected date of confinement was December 22nd. On the morning of September 20th, she went into spontaneous premature labor and simultaneously began bleeding from the vagina. This continued and on the next day vaginal examination was done, which revealed no evidence of placenta previa. By this time the temperature had risen to 101.2 and a cervical smear was obtained which yielded anaerobic streptococci. Labor now progressed more rapidly, and at 4:45 P.M., September 21st, she was delivered spontaneously of a premature child weighing 1325 grams, which succumbed some days later. The temperature and pulse now fell to normal, but on the third day postpartum rose to 103. From this time on the course was febrile, and at about the seventh day after delivery, became hectic in character, with chills and temperature excursions ranging between 98.8 and 103. On September 25th, urine and uterine cultures both yielded anaerobic streptococci. Sulfanilamide therapy was started, but was discontinued after five days, since hemolytic streptococci had not been found and since the drug gave no improvement.

In spite of the apparent severity of the infection, the patient looked and felt remarkably well. However, by October 6th, the hemoglobin had dropped to 54% and a transfusion was given, without reaction. Signs of peritoneal irritation soon developed and the lower abdomen became rigid, with spasm and tenderness, most marked on the left. It seemed evident that the condition present was thrombo-phlebitis, parametritis, and possibly a beginning pelvic abscess. The lungs remained clear. The course, however, was steadily downhill. Multiple chills occurred and the same hectic type of temperature persisted, although for the last 7 days of life the temperature excursions were less, 105 being the approximate level. She was given several transfusions and almost daily intravenous injections of glucose and saline. A palpable mass developed above Poupart's ligament, on the left. Anaerobic streptococci were recovered from the blood stream. Signs of generalized peritonitis became evident, with distention, severe lower abdominal pain, nausea and vomiting. Death occurred on the 38th day postpartum.

Autopsy was obtained, with the following anatomical diagnosis: Pelvic thrombophlebitis and cellulitis. Generalized peritonitis. Septicemia. Terminal bronchopneumonia. Questionable small lung abscesses. (The omentum was markedly thickened and indurated and comprised the previously mentioned abdominal mass.)

*Discussion:* This case is a classical example of pelvic thrombo-phlebitis. As is true of most cases of puerperal infection of this type, the offending agent was the anaerobic streptococcus, an organism which appears to have an especial predilection for veins. The fact that the infection was not affected by the sulfonamides is also characteristic of this bacterium. The multiple chills and the hectic temperature swings, occurring in a patient who looked and felt well, are of course the

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# Gynecology

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## ENDOCRINOLOGY

### A GENERAL SURVEY OF THE VAGINAL SMEAR AND ITS USE IN RESEARCH AND DIAGNOSIS

GEORGE N. PAPANICOLAOU

*Am. J. Obst. & Gynec.*, 51: 316-328, 1946

In this survey of the vaginal smear technique, the author endeavors to give a brief account of some of its applications, more particularly of those related to the human female sex cycle, and to the diagnosis of uterine cancer.

In the earliest attempts to apply the vaginal smear technique in the human, it was found that the striking sequence of clean-cut cytological changes observed and described in the vaginal fluid of the guinea pig and other rodents was practically absent from the human vagina. Therefore, it was not surprising that Allen concluded that "in the primates, menstruation furnishes such a prominent milestone that vaginal smears seem of secondary importance for diagnosis." In contrast to the extensive cornification and massive desquamation of the vaginal epithelium in rodents, the epithelium of the human vagina undergoes only a partial and incomplete cornification and, consequently, only a partial desquamation of its more superficial layers. However, the existence of a vaginal epithelial rhythm has been demonstrated quite conclusively by the study of epithelial biopsies as well as of vaginal smears.

A complete evaluation of the normal sex cycle in women requires an examination of vaginal smears, not only during the follicular and postovulatory stages, but during all phases of the cycle. The structural changes of the vaginal epithelium are particularly distinct during the period of high follicular activity prior to ovulation. Ovulation results in a disruption of follicular growth and is revealed in the smear by distinct modifications in the form and grouping of the exfoliated cells. These changes are the result of the decrease in the secretion of estrin and therefore the vaginal smear offers only indirect evidence as to ovulation and the time of its occurrence.

The extent of the endometrial exfoliation and its duration vary greatly. In anovulatory cycles or in bleedings induced by estrogenic or other therapy, the uterine desquamation is usually less conspicuous than in the normal cycle, and the cells tend to be smaller and more densely grouped.

The use of smears prepared with fluid aspirated either from the cervical canal or from the uterine cavity with the aid of a thin metal cannula has been advocated

labor in the presence of a twin pregnancy is usually unwise. Most of the amniotic fluid in twin pregnancies is in the upper sac and hence puncture of the lower sac releases relatively less fluid than it does in single pregnancies. Moreover, patients with twin pregnancies often exhibit the uterine inertia of over distention and a long latent period may be anticipated. Especially reprehensible was the failure to respect a long, hard, virtually closed cervix. In the presence of such a cervix attempts to induce labor by any known means will often fail. This type of cervix should always be regarded as a contra-indication to the induction of labor, particularly in a case such as this in which early delivery was urgently desirable.

Since eclampsia is 4 to 5 times more common in twin pregnancies than in single, and since this patient became rapidly worse despite treatment, the need for immediate delivery should have been recognized. It is true that cesarean section is performed much too frequently, but in cases in which it is indicated it may be a life-saving procedure, and this case would seem to be one of them.

really an epoch-making one, since it became no longer necessary to depend upon sex behavior or histological studies of the ovaries or genital canal. As a matter of fact, this discovery is largely responsible for the intense interest which anatomists and physiologists have since then shown in the problems of reproductive physiology, in which such brilliant advances have been made.

As applied to the human, however, one cannot say that the yield of results has been anything like as impressive. Not everyone will agree with Papanicolaou that biopsy studies have shown a definite vaginal histological cycle, for there have been many dissenters among well-qualified investigators, such as Zondek, Stieve, and Traut and Kuder. Though it may seem rather paradoxical, everyone will agree that there is a vaginal epithelial rhythm, certainly in so far as estrogen responsiveness is concerned. In the retrospect it would seem that the earlier hopes for the vaginal smear method in the study of functional disorders, or as a guide to their treatment, were too sanguine. As a matter of fact, it is probable that many modern gynecologists will not consider archaic Allen's view that in the human the "occurrence of menstruation furnishes such a prominent milestone that vaginal smears seem of secondary importance for diagnosis." This statement should be supplemented by saying that the endometrium appears to furnish a far more reliable index of ovarian hormone effect than does the vagina, certainly in so far as progesterone is concerned. Endometrial biopsy is exceedingly simple, requiring only a few moments, with no anesthesia and very little discomfort. Many of us will feel that for most of the practical problems encountered in the field of ovarian dysfunctions, a single premenstrual biopsy yields much more information than a long series of vaginal smear studies. In other words, many of us would hate to try to get along without endometrial biopsy, and yet might feel that, in the present state of our knowledge, the patient would not be deprived of anything very important if she did not have the benefit of vaginal smear studies.

These statements are made with full appreciation of the scientific value of vaginal cytology, and of its possibly much greater practical value in the future. In the field of cancer investigation it is possible that the vaginal smear method of study may attain value as a screening test, though it is difficult to believe that it could ever supplant biopsy as a means of decisive diagnosis. Papanicolaou himself is very conservative on this point, urging that for the present the procedure be employed with great discretion. See also editorial comment on this subject in February Survey, p. 106, and June Survey, p. 373.—Ed.)

## REPRODUCTIVE CYCLE. RECENT ADVANCES IN ENDOCRINE PHYSIOLOGY

ALVARO DE AQUINO SALLES

Anais Brasileiros de Ginecologia, 20: No. 4, 1945

In this article the writer makes a review of the more relevant recent laboratory investigations in the endocrine field of gynecology during the last decade, and attempts to furnish a new explanation for the mechanism involved in the menstrual cycle, according to those new clinical and experimental findings.

According to the studies of Greep, van Dyke, Chow, Fevold and Hisaw, the pituitary follicle-stimulating hormone merely promotes the growth and development of the ovarian follicles beyond the time of formation of the "antrum." It does not stimulate the secretion of the gonadal hormones. This is accomplished under the influence of the luteinizing hormone of the pituitary, by the theca cells

by the author and Marchetti. These smears are of value, not only in the study of the normal cycle and of problems relating to ovulation and sterility, but also in the diagnosis of fundal and endocervical neoplasms and of endometritis and hyperplasia.

Changes typical of gestation appear in the vaginal smear as early as the 38th or 40th day. However, it is not always easy to differentiate them from some closely-resembling cell types. Nevertheless, the vaginal smear remains a useful guide in pregnancy. Abnormal features suggestive of threatened abortion may be recognized, such as blood, excessive mucus, pronounced acidophilia or intracellular blood-pigmentation. In abortions there is an increase in the number and the phagocytic action of the histiocytes and the polymorphonuclears. In incomplete abortion, a definite diagnosis can be established when trophoblastic or other placental or fetal cells are found.

Since 1923, the author had been impressed by the strikingly abnormal features of cancer cells and their nuclei, and had become aware of the diagnostic potentialities of the vaginal smear in malignant lesions of the uterus. In 1939, he resumed the cancer work with Traut, and later with Marchetti. The results were published in 1943. Among other investigators, in an evaluation of 813 cases, false negatives were 7.1 per cent and false positives were 2.8 per cent. In another series of 434 cases, false negatives were 7 and false positives were 9. The high percentage of false positives in the latter series indicates that more must be learned about the reliability and the pathognomonic value of some of the criteria. For this reason, the author feels that this diagnostic procedure should at present be employed with great discretion.

The nuclear changes of cancer cells seem to offer the most reliable diagnostic criteria. The nucleus tends to be large and out of proportion to the size of the cell. Many nuclei are hyperchromatic or may show fragmentation. In certain types of cancer, the nucleoli are large and very conspicuous. The interpretation of these smears is rather difficult and requires special study and training.

Marshall and the author have investigated the possibility of detecting carcinomas of the urinary tract in both men and women by examination of smears prepared from urine sediment. From about 120 cases, thus far studied, evidence is presented that neoplasms of the urinary organs, including bladder, prostate and kidneys, can be detected by this method.

In conclusion, the author emphasizes the fact that the smear method is morphologically sound and that it is also short, simple and inexpensive. In cancer diagnosis its reliability and value are being increasingly recognized and it is also particularly adapted to the screening of large numbers of women, as in cancer-prevention clinics.

Discussants on this report are Dr. M. Edward Davis, Dr. Rachmiel Levine, Dr. John F. Sheehan and Dr. Philip H. Schneider. 3 figures.

(The author, who may be looked upon as the father of the vaginal smear method of study, has now for many years been applying this technique to human problems. The demonstration by Papanicolaou and Stoekard in 1917 that the phases of the laboratory animal's estrous cycle were so simply demonstrable by the study of the vaginal cell content was

stimulating and luteinizing gonadotropic hormones reaches a certain level. At this time, under the influence of the luteotrophin, the follicle-stimulating hormone disappears and the corpus luteum grows and secretes progesterone in progressively larger amounts.

Later on, as soon as the progesterone reaches a certain level of concentration, the luteinizing gonadotropic hormone disappears.

Through exhaustion of the luteotrophin hormone, the follicle-stimulating hormone reappears while the corpus luteum undergoes retrogression and menstruation takes place.

(The author has obviously familiarized himself quite thoroughly with new developments in the field of reproductive physiology, and he has attempted to fit these new bits into the jig-saw puzzle of the reproductive mechanism, in spite of the fact that some of the bits are still rough and unfinished. The exact rôle of luteotrophin is still far from being well-established and we do not yet know the exact hormonal mechanism of ovulation. The best evidence available thus far does indicate that the occurrence of ovulation is determined by a certain quantitative balance of the two chief pituitary gonadotrophic principles, presumably a large amount of the follicle-ripening and a small amount of the luteinizing factor. There is good reason also for the view held by many that small amounts of progesterone are released even before ovulation, but the mechanism involved is not clearly established.

Relaxin has been a sort of step-child among the reproductive hormones, and its exact nature is still not altogether clear. Since its original description by Hisaw and his collaborators, it has at various times and by various workers been linked up with estrogen or with progesterone, and its separateness as a hormone principle has not infrequently been denied. Hisaw and his group, however, have consistently maintained that it is a distinctive hormone principle, with a characteristic effect, not possessed by either estrogen or progesterone, of producing relaxation of the subpubic ligament. The fact remains, however, that it has appeared to make no great impression upon concepts of reproductive endocrinology, and certainly has seemed to have no noteworthy clinical implications.

The concept of the menstrual mechanism which Salles hypothesizes is of great interest, but since it includes so many conceptions which are still so imperfectly understood, it must naturally be viewed with much reserve.—Ed.)

## ENDOCRINE ASPECTS OF OBESITY

MAX A. GOLDZIEHER

Am. J. Digest. Dis., 13: 40-54, 1946

According to available records, the anatomical changes of the pituitary and of other endocrine organs, including the thyroid and gonads, are neither consistent nor specific enough to warrant pathogenetic conclusions.

A discussion of the data concerning the metabolic status of the obese is handicapped by the failure of previous investigators to separate "simple" and endocrine cases of obesity. Previous calculations of basal heat production were unmindful of the variable oxygen consumption attendant to anabolic processes in the cytoplasm.

The author presents evidence to show that the adipose tissue is not merely engaged in the passive storage of fat but plays an active metabolic role.

of follicles that have already been stimulated, and by the interfollicular and interstitial cells.

Regarding corpus luteum activity, the chief new concept is that a third pituitary principle seems to be related to it—the luteotrophin, which, according to many investigators, is the same as the lactogenic hormone of the pituitary.

Progesterone seems to be secreted even before ovulation takes place, under the influence of the gonadotropic luteinizing hormone (Dempsey, Astwood, Boling, Barton and Burr). After ovulation, progesterone suppresses the production of the luteinizing hormone. The life and duration of the corpus luteum would depend on the luteotrophin of the pituitary, which probably is secreted during the final stage of proliferation and throughout the whole stage of secretion.

The great differences in opinion regarding the hormone relaxin (Hisaw), and as to whether to consider it a separate hormone or as closely related to progesterone, seem now to be crystallized owing to the studies of Abramowitz, Money, Zarrow, Hisaw, Marder and Sumner (1944). These investigators have demonstrated that while relaxin acts directly on the pelvic ligaments, progesterone does so indirectly by promoting the production of relaxin through the female genital tract. The presence of the latter is necessary for the accomplishment of this function. As a matter of fact, progesterone does not promote relaxation in the castrated and hysterectomized guinea-pig, although relaxin is capable of doing so. Thus, relaxin is neither progesterone nor estrogen; it is a hormone related in some way to luteal activity. However, estrogens seem also to collaborate with relaxin in promoting relaxation of the pelvis.

Estrogens in small doses stimulate the functional activity of the basophilic cells of the anterior pituitary, and in high doses the eosinophilic cells also, thus liberating the luteinizing principle. This can be seen in cases of hyperplasia of the endometrium treated with large doses of stilbestrol (Abarbanel). It is in accordance with the results of cytologic examinations of the anterior pituitary carried out during the climacteric period, but it goes against the generally accepted idea that large amounts of estrogen inhibit the anterior hypophysis.

Estrogens can exert a luteotrophic effect if the pituitary is present. Hence, it is probable that estrogens secreted during the proliferative stage of the menstrual cycle stimulate the production of the luteotrophin hormone of the pituitary.

On the basis of these findings, the author presents a new hypothetical explanation for the complex interglandular relationship involved in the mechanism of the menstrual cycle.

Through the influence of the follicle-stimulating hormone of the pituitary, which is being secreted since the final stage of the secretory stage, the ovarian follicles develop, and under the simultaneous activity of the luteinizing gonadotropic hormone, still in insufficient amounts to promote ovulation, secrete estrogens. Stimulated by the latter, the luteinizing hormone of the pituitary is produced in progressively higher amounts, thus promoting the partial luteinization of the thecal cells of certain mature follicles. Then, still under the same estrogenic stimulus, a small amount of luteotrophin is released from the hypophysis prior to ovulation, which takes place as soon as the balance of both follicle-

## THE EFFECT OF THE ADMINISTRATION OF ESTROGENS UPON THE PRODUCTION OF CERVICAL MUCUS IN CASTRATED WOMEN

W. T. POMMERENKE AND ELLENMAE VIERGIVER

J. Clin. Endocrinol., 6: 99-108, 1946

The authors have studied the effect of the administration of various hormones on cervical mucus in 5 recently castrated women, 4 of whom had also undergone supracervical hysterectomy. The ages of these women ranged from 19 to 35 years. Following castration, the amount of mucus coming from the cervix is very scanty and opalescent.

Observations were started from 4 to 7 weeks postoperatively and each individual was given approximately the same course of therapy. Examinations were made on alternate days, at which time the mucus present at the external os of the cervix and that from the lower portion of the cervical canal was aspirated with a cannula. Vaginal smears were taken at each examination and were stained by the Shorr technic. The viscosity of the cervical mucus was determined by estimating the ease with which it could be drawn up into a capillary tube of about 0.4 mm. diameter.

The administration of progesterone was noted to be without effect on the amount of mucus secreted.

The injection of alpha-estradiol benzoate was followed by a significant increase in the amount and the translucency of the mucus, dependent in part upon the amount of hormone administered. The daily administration of diethylstilbestrol dipropionate gave results comparable to those obtained following the single injections of larger amounts of alpha-estradiol benzoate.

All but one of the subjects showed a good response in the vaginal smear following the injections of 3.32 and 1.66 mg. of estradiol and all the subjects showed good response during the period of daily administration of 0.25 and 0.5 mg. of stilbestrol.

The authors suggest, as did Bennett, that a study of the cervical mucus be employed for objectively appraising the effect of estrogen therapy in women at the menopause.

(This paper supplements one published by the same authors very recently (Am. J. Obst. & Gynec., 51: 192 (Feb.), 1946) and abstracted, with editorial comment, in the June Survey (p. 445). The present study indicates the undoubted influence of estrogen in increasing the amount and translucency of the cervical mucus, though it throws no light on the effect of progesterone, which apparently plays some part in the normal histological cycle in the cervix, as suggested by the studies of Sjövall, the best as yet made on this poorly understood subject. As bearing on the effects of estrogen, I have noted that women with hyperplasia of the endometrium and functional bleeding often have a rather free mucoid cervical discharge, apparently due to hyperactivity of the cervical glands, in the absence of any infection.—Ed.)

Deposit of fat is the consequence of food intake beyond the limits of the body's ability to increase energy consumption; loss of depot fat occurs if the caloric deficit is greater than the ability of the body to restrain metabolic activities. The mechanism regulating the diversified metabolic activities, including the specific dynamic action of proteins, luxury consumption and cellular anabolism, is controlled to a large extent by the endocrine glands.

The active function of the fat tissue, which includes formation and storage of fat as well as its mobilization and metabolic utilization, is demonstrably under the influence of the endocrine glands.

Retention of water and salt is an important contributory factor in obesity; the author presents evidence indicating that salt and water metabolism is regulated by endocrine influences.

A tendency to obesity and to increased regional fat deposits is hereditary. The genetic transmission of these tendencies is frequently associated with similarly inherited peculiarities of the endocrine glands.

The onset of obesity frequently coincides with manifest changes in the activity of the endocrine system or with events likely to affect one or several endocrine organs.

Weight reduction can be accomplished by diet alone, provided the caloric intake is low enough. Better clinical results are obtained with less rigorous restriction of food intake if suitable endocrine therapy is added; regional fat deposits also yield better to such combined treatment than to mere dietary weight reduction.

(Obesity is such a common accompaniment of some of the endocrinopathies constantly encountered by the gynecologist that the latter must have at least some idea as to its possible causes and management. In a considerable proportion of cases, the cause is exogenous, due simply to overeating. In other cases, endocrine factors are responsible, especially those referable to the thyroid, the ovaries and the pituitary. However, as regards the latter, there is good evidence that in the so-called pituitary type of adiposity, the cause lies not in the pituitary itself, but in the fat-metabolism centres located in the par-pituitary, probably hypothalamic areas of the brain. This is probably the explanation of the characteristic type of obesity seen in the common adiposo-genital dystrophy, or Fröhlich's disease. Again, in many of the most extreme types of obesity, as in some of the circus "fat ladies", it is probable that the cause is purely cerebral rather than of endocrine type.)

Finally, as in the not infrequent cases of familial obesity, in which the hereditary factor seems clearly apparent, we must fall back on the chromosomal or constitutional explanation. With obesity, as with so many other conditions which parade themselves as endocrinopathies, it is really this constitutional or chromosomal factor which is often responsible.

I do not know whether or not the adipose tissue actually plays an active metabolic rôle, as Goldzieher suggests. But there seems to be no doubt that reduction of weight in obese women, entirely aside from all esthetic considerations, does actually promote a readjustment of disordered endocrine mechanisms. In the common adiposo-genital type, for example, amenorrhea is often seen. Mere restriction of diet, with the resulting loss in weight, will often be followed by reestablishment of the menstrual function. Whatever other treatment, with thyroid or other hormones, may be employed, it should certainly be combined with caloric dietary restriction.—Ed.)

mized rat. The following is a summary of the author's ideas, together with certain experimental data and predictions that have been made:

A given substance may be estrogenic if it consists of a rather large, rigid and inert molecular structure with 2 active hydrogen bond-forming groups (e.g., phenolic hydroxyl groups) located at an optimum distance of 8.55 Å. from one another. In particular, the substance *trans*-*p,p'*-dihydroxyazobenzene meets the requirements for an estrogen and, in spite of its obvious chemical and physical differences from the natural and synthetic estrogens, shows definite estrogenic activity in dosages of from 10 to 15 mg. injected subcutaneously into spayed rats and in much smaller dosages when applied directly to the vagina.

If the active groups are at a distance of approximately 9–10 Å. and are of somewhat weaker hydrogen bond-forming character (e.g., secondary alcoholic hydroxyl groups), then the substance may have an androgenic activity. The prediction is made, upon the basis of this hypothesis, that certain nonsteroid substances will show male hormonal activity (e.g., the perhydro derivatives of *trans*-diethylstilbestrol and perhydro-2(*p*-hydroxyphenyl)-6-hydroxynaphthalene). It is also noted that the dosage required to produce an androgenic effect in rats by the most active androgens is vastly greater than the quantity of estrogen needed to produce estrus in the rat. This may be explained by the greater hydrogen bond-forming power of "estrogenic hydrogen" (which is usually due to phenolic —OH groups) as compared to the weaker hydrogen bond-forming power of the androgenic hydrogen (e.g., secondary alcoholic hydrogen).

(I know too little of the intricacies of organic chemistry to comment on this paper intelligently, except to say that it appears to indicate that the male and female sex hormones are perhaps not as antithetic as some appear to think them, and that they are closely akin chemically, with a considerable degree of intermutability. To this may be added such facts as that one and the same gonad may produce either the male or female hormone, that there is a curve of androgenic hormone in the blood of women during reproductive life just as there is an estrogen curve, that the urine of some men contains estrogen, and that a rich source of estrogen is the testis of the stallion, etc. I mention these facts because some endocrinologists look with horror upon the use of even small doses of testosterone in women, seeming to consider it about as much of a contaminating factor to the female as the vaginal injection of spermatozoa. To this extreme view I do not subscribe.—Ed.)

## ENDOCRINE DISORDERS AS RELATED TO PELVIC PAIN

R. G. CULLEY

Kentucky M. J., 44: 149–150, 1946

The author summarizes the causes of pelvic pain due to endocrine disorders in the following manner:

(i) *Fatigued patients:* These individuals are usually highly emotional and tend to extend their energies to the point of fatigue which creates nervous instability, which in turn exaggerates physical pain.

## OVULATORY CYCLE IN THE CERVIX OF THE MONKEY

CLARA E. HAMILTON

*Anat. Rec.*, 94: 466, 1946

Forty-eight normal female monkeys with regular, ovulatory menstrual cycles were studied. Measurements were made of epithelial cells lining the cervical canal and of epithelial cells lining the cervical glands. Peaks in cell heights fall on days 3, 13-14, and 22, the greatest of these on days 13-14. Curves of the mucosal growth and regression closely parallel Markee and Berg's ('44) blood estrogen level curve which they determined from women with apparently normal cycles. Assuming that the estrogen level in monkeys follows a similar curve to that in women, it would seem that the growth and regression of the cells of the cervical mucosa are due to the action of estrogen. When superimposed on the blood estrogen curve of women, the cervical curves of the monkey show a definite, regular lag which may be the latent period necessary for response. The peaks in the two curves are closely correlated in point of time and their relative quantitative increases correspond.

Leucocytes are most abundant in the wall and lumen of the cervix during the menstrual period. They are also abundant several days before and after ovulation. The cervical glands are most highly proliferated in the post ovulatory period. Examination of the series shows much secretion around the middle of the cycle but the accumulation of mucus in the cervical lumen and crypts seems greatest on days 22-24.

(This work would seem to indicate that the changes in cervical cell height and other cyclical cervical changes are due entirely to the influence of estrogen, no rôle being ascribed to progesterone. In this respect the findings differ from those of the Scandinavian investigator, Sjövall, whose studies on the cervical cycle are, to my mind, the most complete of any as yet made (*Acta obst. et gynec.*, suppl. 4, Scandinav., 18: 4, 1932). According to Sjövall, there is a postovulatory decrease in the height of the cervical epithelium as a result of progesterone influence. There is still need of further study on this subject. The investigations of Wollner, frequently quoted, were based on too small a material to be of any real value. More progress has apparently been made in the study of cyclical changes in the cervical mucus than in the study of the cyclical histology of the cervical mucosa.—Ed.)

## SEX HORMONAL ACTION AND CHEMICAL CONSTITUTION

F. W. SCHUELER

*Science*, 103: 221-223, 1946

This paper presents a new hypothesis regarding the essential chemical and structural features sufficient for male and female sex hormonal activity as evidenced by comb growth in the capon and production of estrus in the ovariecto-

mized rat. The following is a summary of the author's ideas, together with certain experimental data and predictions that have been made:

A given substance may be estrogenic if it consists of a rather large, rigid and inert molecular structure with 2 active hydrogen bond-forming groups (e.g., phenolic hydroxyl groups) located at an optimum distance of 8.55 Å. from one another. In particular, the substance *trans-p,p'*-dihydroxyazobenzene meets the requirements for an estrogen and, in spite of its obvious chemical and physical differences from the natural and synthetic estrogens, shows definite estrogenic activity in dosages of from 10 to 15 mg. injected subcutaneously into spayed rats and in much smaller dosages when applied directly to the vagina.

If the active groups are at a distance of approximately 9–10 Å. and are of somewhat weaker hydrogen bond-forming character (e.g., secondary alcoholic hydroxyl groups), then the substance may have an androgenic activity. The prediction is made, upon the basis of this hypothesis, that certain nonsteroid substances will show male hormonal activity (e.g., the perhydro derivatives of *trans*-diethylstilbestrol and perhydro-2(*p*-hydroxyphenyl)-6-hydroxynaphthalene). It is also noted that the dosage required to produce an androgenic effect in rats by the most active androgens is vastly greater than the quantity of estrogen needed to produce estrus in the rat. This may be explained by the greater hydrogen bond-forming power of "estrogenic hydrogen" (which is usually due to phenolic —OH groups) as compared to the weaker hydrogen bond-forming power of the androgenic hydrogen (e.g., secondary alcoholic hydrogen).

(I know too little of the intricacies of organic chemistry to comment on this paper intelligently, except to say that it appears to indicate that the male and female sex hormones are perhaps not as antithetic as some appear to think them, and that they are closely akin chemically, with a considerable degree of intermutability. To this may be added such facts as that one and the same gonad may produce either the male or female hormone, that there is a curve of androgenic hormone in the blood of women during reproductive life just as there is an estrogen curve, that the urine of some men contains estrogen, and that a rich source of estrogen is the testis of the stallion, etc. I mention these facts because some endocrinologists look with horror upon the use of even small doses of testosterone in women, seeming to consider it about as much of a contaminating factor to the female as the vaginal injection of spermatozoa. To this extreme view I do not subscribe.—Ed.)

## ENDOCRINE DISORDERS AS RELATED TO PELVIC PAIN

R. G. CULLEY

Kentucky M. J., 44: 149–150, 1946

The author summarizes the causes of pelvic pain due to endocrine disorders in the following manner:

(1) *Fatigued patients:* These individuals are usually highly emotional and tend to extend their energies to the point of fatigue which creates nervous instability, which in turn exaggerates physical pain.

(2) **Dysmenorrhea:** Some patients may suffer with pain from dysmenorrhea caused by hypothyroidism and hypopituitary functions.

(3) **Primary hypo-ovarianism:** This is usually due to the menopause or to a primary ovarian dysfunction. The common cause in younger women is pelvic pathology.

(4) **Intermenstrual pain:** Nearly all of these cases are sterile. There is usually pelvic pathology, either fibroid uterus or ovarian endometriosis. No endocrine therapy is satisfactory in these cases.

(5) **Painful intercourse:** This is usually due to some pathology present, but in about 10 per cent of cases it is due to an endocrine disturbance.

(This is a rather trite and superficial review, and not all the conclusions are sound. I know of no evidence, for example, that primary dysmenorrhea is often caused by hypothyroidism or hypopituitarism, or that primary hypo-ovarianism in either young or old women is generally due to pelvic pathology. If by intermenstrual pain the author means persistent pelvic discomfort and not the so-called "mittelschmerz", it is true that pelvic pathology of some sort is often, though not by any means always, present, and that endocrine therapy would be as foolish as it is futile. Finally, I wonder what sort of endocrine disturbance the author has in mind in the explanation of 10 per cent of cases of dyspareunia.—Ed.)

## OVARIAN INFLUENCE OF THE RESPONSE OF THE ANTERIOR PITUITARY TO ESTROGENS

J. T. BRADBURY

Anat. Rec., 94: 450, 1946

The gonadotrophic potency of the pituitary of immature female rats has been determined after 3 to 6 days of treatment with estrogens. (Estrone, estradiol and stilbestrol, in total doses ranging from 2 gamma to 50 gamma). The average pituitary weight increases from about 2.5 to 3.0 mg as a result of estrogen treatment. There is a marked loss of gonadotrophic hormone from the pituitary of normal females treated with estrogen. There is a significant increase in ovarian weights after injection of estrogen; control ovaries 14 mg, treated 22 mg. This increase in weight is due primarily to an increase in interstitial tissue. Progesterone given together with the estrogen prevents the loss of pituitary potency and also the increase in ovarian weight which is produced by estrogen alone.

When rats are ovariectomized a day or two before estrogen is given, there is a comparable increase in pituitary weight but there is no demonstrable loss in gonadotrophic potency. The results indicate that the presence of the ovary facilitates the action of estrogen in the pituitary. Furthermore, the factor in the ovary is neither estrogen nor progestin.

(While there has been some evidence to suggest that moderate dosage of estrogen may actually stimulate the pituitary gonadotrophic function, the weight of available evidence

is that in general the effects of estrogen upon the gonadotrophins are inhibitory. Upon this concept of a reverse effect of ovarian hormones upon the pituitary, as a matter of fact, are built up our concepts of the interlocking mechanism of the two glands in the phenomena of the reproductive cycle, as well as our explanations of certain menstrual disorders, especially functional bleeding.

Of special interest in Bradbury's study is that estrogen administration produces no loss in gonadotrophic potency if the animals have been previously ovariectomized, and that neither estrogen nor progesterone is responsible for this negation of estrogen effect. This rather surprising result seems worthy of further investigation.—Ed.)

## THE EFFECT OF THE CORPUS LUTEUM HORMONE UPON THE UTERUS OF THE DEVELOPING OPOSSUM, DIDELPHYS VIRGINIANA

O. E. NELSEN

Anat. Rec., 94: 409-410, 1946

During the development of the female opossum, the response of the uterus to the corpus luteum hormone appears to be as follows:

(a) The uteri of animals 3 months and younger fail to show a detectable response.

(b) The uteri of animals of 4 to 8 months manifest a slight response of the uterine glandular epithelium, evidenced by an increase in the height of some of the cells, and by a tendency of the nuclei to be situated basally. This suggests a transformation in the direction of typically developed glandular epithelium. The external morphology shows little, if any, change.

(c) In young females of the first anestrus, and in older females during anestrus, a response similar to that of group (b) above may be noted. The older females show much variation in the degree of response, some demonstrating well developed glandular epithelium in the uterine glands.

(d) When any of the above groups are stimulated first with estrogenic substance followed by the corpus luteum hormone, the response is immediate and marked. These general results point to the assumption that the young female opossum begins to secrete a small amount of estrogenic substance at about the fourth month of development. This minimal secretion is continued, probably, more or less during its entire reproductive life, including the anestrus periods.

(2) Dysmenorrhea: Some patients may suffer with pain from dysmenorrhea caused by hypothyroidism and hypopituitary functions.

(3) Primary hypo-ovarianism: This is usually due to the menopause or to a primary ovarian dysfunction. The common cause in younger women is pelvic pathology.

(4) Intermenstrual pain: Nearly all of these cases are sterile. There is usually pelvic pathology, either fibroid uterus or ovarian endometriosis. No endocrine therapy is satisfactory in these cases.

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## MENSTRUAL DISORDERS

C. G. SARAIYA

J. Indian M. A., 15: 108-111, 1946

The author reviews the present day concepts of the physiology of the menstrual cycle. It is noted that the theories that menstruation and bleeding are due to (1) withdrawal of estrogen, or (2) withdrawal of progesterone, or (3) some change in the proportions of the 2, are all inadequate. Also, the exact relationship between the suprarenal and thyroid glands and the normal menstrual cycle is not known. Zondek and other workers have postulated the existence of an endometrial factor in producing menstrual bleeding.

Amenorrhea is a symptom due to many causes which the author briefly discusses. In cases of secondary amenorrhea one must rule out pregnancy, lactation and menopause. Pathological amenorrhea may be caused by acute infections, prolonged suppuration, anemias, pulmonary tuberculosis or physical or mental shocks. Amenorrhea may be of pituitary, ovarian or uterine origin. The treatment of amenorrhea may consist of estrogen 5 mgm. twice a week intramuscularly for 2 weeks, followed by progesterone 5 mgm. twice a week for the next 2 weeks. Occasionally menstrual rhythm may be re-established following this treatment.

The author discusses dysmenorrhea and its treatment, emphasizing the importance of mental and bodily fitness, diet, exercise and attention to the psychoneurotic factor. If the uterus is underdeveloped, estrogen and progesterone therapy is suggested. Testosterone has yielded more gratifying results than progesterone. Dilatation of the cervix will cure 60 to 70 per cent of cases. In a very small number of cases, presacral sympathectomy is justified.

The author believes that headache in women is caused, in the majority of cases, by faulty posture, or sacroiliac strain, or neurosis. The gynecological lesions which do cause headache, such as endometriosis, also present other symptoms which in themselves call for treatment.

In cases of dysfunctional uterine bleeding one must first rule out constitutional causes such as purpura, local organic lesions such as fibroids or carcinoma, and complications of pregnancy such as abortions. In puberty cases of dysfunctional uterine bleeding, hormonal treatment has advantages over such forms of treatment as operation and curettage. In all cases except puberty cases curettage should be done to exclude submucous fibroid, mucous polypus or fundal malignancy. This procedure suffices as a temporary measure in many cases. Intra-uterine application of radium may be used in younger women to produce temporary amenorrhea. Hysterectomy may be necessary, especially in women over 40 years of age.

In connection with the treatment of menopausal symptoms, the author refers to 2 points:

(1) It is best to give large doses of estrogens first and, when the symptoms have been controlled, to diminish the dose gradually.

## THE MENSTRUAL CYCLE

### PHASES OF THE MENSTRUAL CYCLE IN THE MACAQUE MONKEY

G. W. BARTELMEZ, G. W. CORNER AND C. G. HARTMAN

Anat. Rec., 94: 512, 1946

One hundred and ninety-seven cases were arranged in groups on the basis of observed menstrual periods, the study of both ovaries or in cases of early pregnancies, the age of the embryos; sometimes the day of ovulation was known. The histologic characters of the endometrium common to the majority of each group were taken as distinctive of the particular group and used to reconstruct the sequence of events in the endometrial cycle. This procedure introduces some objectivity in contrast to the scriations of human material in which subjective factors play a greater role.

The follicular phase (I) begins when activity is initiated postmenstrually, and ends after the vascularization of the corpus luteum has begun. During this phase there is a reorganization of two-thirds or more of the endometrium, mitotic activity is prominent, glycogen and a mucoid are produced by the epithelial cells. The lutein phase (II) is characterized by an increased rate of secretion with retention of secretion in the glands, by the accumulation of oedema fluid and the gradual reduction in the number of mitoses. Evidences of regression mark the ischaemic phase (IV). This is followed by the extravasation and bleeding of the menstrual phase (V). There is a brief phase of postmenstrual repair (VI). The duration of the various phases appears to be as variable as that of the cycle as a whole.

(This contribution by the three leading students of the reproductive cycle in monkeys, presents a complete and authoritative summary of the subject, and, so far as we know, the description of the monkey cycle would apply also to the human. I note that they consider that the follicular phase does not end until the vascularization of the corpus luteum, thus placing the earliest stage of the corpus, that of hyperemia or proliferation, within this follicular phase. In this respect their division of phases differs from that originally laid out for the human cycle by Robert Meyer. From the standpoint of physiology the plan of the authors is certainly the more natural one, as the physiological life of the corpus does not begin until its vascularization is under way. The earliest stage of the corpus is a very short one, so that the time difference in the two plans of classification is not great. Another point of interest is that the authors of this paper find that glycogen and a mucoid are formed in the follicular phase, though their production is greatly increased in the lutein phase, to which many have thought that secretory activity is entirely limited. This question is of great importance to those of us who try to distinguish between secretory and non-secretory endometria obtained by biopsy. As a rule the distinction is easy enough on histological grounds, when the endometrium is obtained shortly before menstruation, but it may be difficult when the tissue examined is obtained at or just after the mid-interval phase. There is evidence, which this paper apparently supports, that the subnuclear vacuoles which many consider valid evidence of secretory or progesterone activity may be produced by estrogen alone (Hisaw).—Ed.)

tropic hormones and, rarely, ovarian masculinizing tumors. Simple obesity may gradually bring about cessation of the menses. Both hypothyroid and hyperthyroid states may result in the absence of the menses. Undernourishment and simple psychic disturbances are causes of amenorrhea and often are found in combination. Adrenal cortical tumors and hyperplasia often result in ovarian disorders, principally amenorrhea. Examination of the urinary ketosteroids often aids in the diagnosis of adrenal cortex activity.

The causes of abnormal hypomenorrhea are essentially those for amenorrhea and this should be considered, therefore, as a phase in the development of amenorrhea. Oligomenorrhea, signifying infrequent menstruation, may be consistent with normal ovarian function or it may be a phase in the development of amenorrhea.

The author discusses the numerous procedures and methods important in the diagnosis of amenorrhea. A thorough history and physical examination should be obtained. In addition to routine laboratory studies of the blood and urine, a number of other tests are important. The x-ray must ascertain the bone age of the individual. Endometrial studies are far more important than practically any other test for ovarian function. Vaginal smears are a fairly reliable index of ovarian function in the hands of experienced workers. Hormonal assays are not of great practical value but the most important practical assay is that of the gonadotropic hormone. Where pregnandiol is found, one may assume fairly safely that a corpus luteum is functioning.

In the treatment of the amenorrhea, psychogenic amenorrhea usually responds very well to psychotherapy. Before treating other types of amenorrhea it is essential to restore the nutritional condition of the patient to normal. In cases where obesity is associated with amenorrhea the patient should be placed on a reducing diet.

Estrogen therapy is the mainstay in the treatment of amenorrhea. In the hypohormonal states, a sufficient amount of estrogen therapy will induce uterine bleeding. In hyperhormonal amenorrhea, if anatomical lesions such as cysts, tumors, etc., are the cause of this state, they should be treated in the appropriate manner. Some authors have experienced satisfactory results in various types of amenorrhea by the use of x-ray to the pituitary gland or to the ovaries.

(While offering nothing new, this paper presents a rather satisfactory review of the quantitative menstrual deficiencies. While our knowledge of the endocrine mechanism is still very incomplete, we are even more inadequate in our methods of treatment when the latter is indicated, as it so often is in those frequent cases in which sterility is an accompanying feature of the amenorrhea.—Ed.)

(2) All symptoms occurring at the menopause are not necessarily due to the menopause and a thorough examination should precede the treatment of supposed menopausal symptoms.

(While the existence of a positive bleeding factor has been suggested by Zondek and others to explain the bleeding of menstruation, there is as yet no proof of this. Hartman, who had expressed such a view even before Zondek, later abandoned it. The late Edger Allen was always a staunch supporter of the estrogen-withdrawal explanation of even menstrual bleeding. There is no doubt that estrogen withdrawal in itself can precipitate uterine bleeding, as many doctors are now demonstrating throughout the country by giving excessive or too long dosage to menopausal patients of stilbestrol and other estrogens, with resulting uterine bleeding.

The weight of evidence indicates, however, that withdrawal of progesterone, rather than estrogen, is the important factor in initiating the bleeding of the normal ovulatory menstrual cycle. The author presents a satisfactory short review of his subject matter, though not all his statements will be accepted. For example, it appears rather optimistic to state that dilatation of the cervix will cure 60 to 70 per cent of dysmenorrhea cases. Intrauterine radium should certainly not be used for functional bleeding in young women unless other more conservative measures fail to help. Again, hysterectomy in women over 40 is not usually indicated unless there is some other reason for opening the abdomen, since x-ray induction of the menopause is so uniformly successful.—Ed.)

## MENSTRUAL DYSFUNCTIONS; AMENORRHEA, OLIGOMENORRHEA, AND HYPOMENORRHEA

S. CHARLES FREED

West. J. Surg., 54: 1-9, 1946

Amenorrhea, signifying the absence of menstrual flow, may be divided into 2 main types—physiologic and nonphysiologic. Physiologic amenorrhea is that which occurs before puberty, during pregnancy and lactation and in the post-menopausal years.

Nonphysiologic amenorrhea may be classified as hyperhormonal amenorrhea and hypohormonal amenorrhea. Persistently elevated blood levels of estrogen which do not drop past the bleeding threshold prevent uterine bleeding and result in hyperhormonal amenorrhea. Numerous small ovarian cysts containing active follicular cells or a granulosa cell tumor may secrete sufficient estrogen to maintain the level above that of the bleeding threshold. Corpus luteum cysts, a deficiency of the Vitamin B complex and cirrhosis or hepatitis will often result in amenorrhea.

In considering hypohormonal amenorrhea, disorders of the anterior pituitary which result in an inadequate secretion of gonadotropic hormone and the failure, therefore, to stimulate the secretion of estrogen, may result in amenorrhea. Ovarian causes include a subnormal amount of estrogenic ovarian secretion, complete absence of the ovary, lack of response of the ovarian tissue to the gonado-

one knows the exact association pathways involved. This general statement would probably not provoke much debate, but not many will feel that Sher has any worthwhile evidence to justify his hypothesis as to the mechanism involved.—Ed.)

## STUDIES ON HIGH DOSAGE PROGESTERONE THERAPY OF AMENORRHEA

A. E. RAKOFF

Am. J. Obst. & Gynec., 51: 480-491, 1946

The author presents the results in a total of 51 amenorrheic patients who were treated with high dosage progesterone with or without additional estrogen. Seven of the patients had primary amenorrhea; the remaining 44 patients had secondary amenorrhea. In 25 cases the amenorrhea was of more than 2 years' duration. From the endocrine standpoint, 18 of the patients had gonadotropic deficiencies; 28 of the patients had a primary ovarian deficiency. Four patients were believed to have an adrenogenital syndrome, and one patient had a primary uterine defect.

In the 25 patients with amenorrhea of more than 2 years' duration, only 5, or 20 per cent, responded with bleeding to progesterone alone, whereas 24, or 96 per cent, of the 26 patients with amenorrhea of lesser duration bled.

None of the 7 patients with primary amenorrhea had bleeding after 60 mg. of progesterone, while 5 of the 6 who were given progesterone after estrogen priming had induced bleeding. Only one spontaneous bleeding occurred after withdrawal therapy. The patient who failed to respond at all had an endometrial defect.

Of the 44 patients with secondary amenorrhea, 29, or 66 per cent, responded to progesterone alone. Many of these had subsequent spontaneous bleedings, and 5 became pregnant. The remaining 15 patients had induced bleeding with progesterone after estrogen priming. A smaller percentage of these patients had subsequent cycles and only one became pregnant.

The patients with a gonadotropic deficiency and those with a primary ovarian deficiency responded approximately equally well so far as induction of bleeding was concerned. In both of these groups there was a tendency for the hormonal status to improve immediately following treatment as indicated by increased gonadotropic production in the first group and better ovarian response (increased estrogens and improved endometrium) in the second group.

Four patients with secondary amenorrhea due to adrenogenital syndrome responded with bleeding to progesterone therapy alone, even if the amenorrhea was of long duration. The endocrine status of these patients did not improve.

Eight, or 27 per cent, of the 30 married women became pregnant following therapy.

An additional group of 18 patients with delayed menstruation or recent

## CAUSES OF DELAYED MENSTRUATION AND ITS TREATMENT; AN INVESTIGATION IN THE WOMEN'S AUXILIARY AIR FORCE

N. SHER.

Brit. M. J., 1: 347-349, 1946

The incidence of delayed menstruation among 2312 airwomen was calculated by the author. The total number of cases of amenorrhea in this series was 139. It was found that sedentary workers were mainly affected. The duration of the amenorrhea varied from one to 7 months, 44.64 per cent of the women having had a delay of 3 months and only 2.15 per cent having had a delay of 7 months.

The diets of the Royal Air Force stations were examined in order to investigate Teebken's contention that a deficiency in protein is one of the most important factors in the production of delayed menstruation. This theory was disproved, as it was found that the quantity of protein in the diet was sufficient for an airwoman of average weight.

Carbaminocholine chloride was administered to 8 patients with the result that 7 of these menstruated. One patient bled with placebo therapy alone.

In an effort to explain the cessation of the bleeding phase of the menstrual cycle in a healthy young woman, resulting from a sudden change in environment, the author postulates an interesting hypothesis which, if not yet valid, is at least in accord with fact. The following experimental evidence is presented:

(1) The hypothalamus probably governs our emotional response to external environment, that response being expressed through the hypothalamic-sympathetic and parasympathetic nervous system connections.

(2) Hypothalamic stimulation produces autonomic discharge, the final effect being dependent on the preponderance of the sympathetic or parasympathetic nerve fibers.

(3) The injection of estrone in ovariectomized animals causes a hyperemia of the uterus and an increase in its acetylcholine content. Bleeding may depend on the presence of the latter.

(4) Luteinizing hormone is released from the anterior hypophysis by an acetylcholine-like substance, liberated by the hypothalamus.

On the basis of these facts, it is concluded that environmental stress or psychic trauma, no matter what its origin, will activate the hypothalamus to produce adrenalin and acetylcholine. Should the sympathetic fibers predominate, however, then a relative deficiency of acetylcholine will be present and thus bleeding will be suppressed, owing to either: (a) a local deficiency of acetylcholine in the uterus, or (b) absence of luteal hormone and consequently of corpora lutea.

(There is much reason to believe that, of all the endocrine glands, it is the pituitary through which environmental and psychic factors affect the reproductive cycle, as they undoubtedly do in some cases. The amenorrhea produced by change of climate, or by such factors as intense apprehensiveness as to the existence of pregnancy or intense longing for the latter, are good examples. It seems highly probable that the liason between the higher centers, as well as with the hypothalamus, is by way of the pituitary, although no

strength of the spasm which is caused by the stimulus; and (3) the strength of the pain sensation which is caused by the spasm. This accounts for the great variety of "menstrual conditions" in adolescents.

In regard to willpower, the factors to be considered in dysmenorrhea are hormonal chemistry, spasms and sensation of pain. The influence of will upon hormonal chemistry can be disregarded in this connection. However, the influence of will upon spasms is a very different matter. It is well known that an excited state of mind, which pays anxious attention to the disturbance, increases spasms. A calm state of mind or a diverted mind decreases spasms or keeps them at a minimum. Yet the spasm and the pain are not identical in strength. The spasm comes from the abdominal cavity; the pain comes about in the brain. All pain is felt by cooperation of thalamus and cortex. Willpower may try to disregard the disturbance in the thalamus and to forget about the pain.

In physical education and sports, it conforms with the best medical rules to minimize the significance of menstruation, of dysmenorrhoeic discomfort and, in most cases, of dysmenorrhoeic pain. However, it should not be forgotten that there are very great individual differences in the menstrual condition and in the strength of pain.

The treatment of secondary dysmenorrhea belongs to the physician exclusively. Therapy for primary dysmenorrhea has the choice of hormonal treatment, antispasmodics, analgesics and psychological treatment. The psychological treatment plays by far the greatest role in the routine of schools, colleges and other organizations which deal with large numbers of young women.

The basic problem in physical education is the question: Is physical exercise liable to harm the pelvic health of a girl? The author answers that physical exercise does not cause pelvic damage in young women, nor does it cause conditions for later dysmenorrhea. Another question concerns the role of physical exercise in the prevention and cure of dysmenorrhea. The physician knows the value of the physical and psychological strengthening, which are the objectives of physical education, in combatting dysmenorrhea. However, he does not believe that one single method can prevent or cure dysmenorrhea.

At one time, girls were excluded from physical education during menstruation. Now the tendency is developing from as little routine excuse as possible to no routine excuse at all. From the medical point of view, the former attitude was sounder in many respects. Surgery is not performed during a menstrual period if the case is not urgent. The physician does not understand why sports and physical education should take chances with a physical complication that medicine is eager to dodge. The sports leader, as well as the physician, should be aware of the value of psychological conditioning but also of the enormous complexity of dysmenorrhea.

(The author states that the available methods of therapy for primary dysmenorrhea are hormone treatment, antispasmodics, analgesics and psychological treatment, but as regards their probable relative value the order could be reversed. Certainly the physician who at once begins to think about hormones is apt to be a poor doctor, and to have few successes. In no other gynecological disorder is it so important to treat the patient—the

amenorrhea who were suspected of pregnancy were treated with 40 to 60 mg. of progesterone, 20 mg. on 2 or 3 successive days. As checked by the Friedman test, bleeding failed to occur if pregnancy was present, whereas in all but one instance bleeding was induced in the non-pregnant patients.

(While the publication of Zondek's original paper on the induction of bleeding in amenorrhea by means of progesterone alone or progesterone with preliminary estrogen excited a good deal of interest, the method does not seem to have established itself as of any impressive value in the treatment of amenorrhea. If one may judge from the literature, it frequently fails to induce bleeding, and far more often is not followed by spontaneous menstrual cycles. As with all other methods of therapy, the successes with primary amenorrhea are far fewer than with the secondary variety, and this is borne out in Rakoff's report. When menstruation is apparently re-established by organotherapy in secondary amenorrhea of younger patients, one must be cautious in ascribing the results to the treatment, since spontaneous re-establishment of the function occurs so frequently.—Ed.)

## DYSMENORRHEA AND PHYSICAL EDUCATION

FRANZ SCHUCK

Arch. Pediat., 63: 8-22, 1946

This paper deals with dysmenorrheic disturbances of adolescents and young adults and with their handling in physical education. Physical education and sports need a basis for their everyday actions and this basis should conform with the concepts of modern medicine.

Cases of "secondary" dysmenorrhea, caused by some pathological lesion, are few if compared with the number of students who suffer from dysmenorrhea. However, the physical educator must constantly be aware of their existence. It may be stated that physical education and sports are mainly confronted with the problem of "primary" dysmenorrhea, in which there is no traceable lesion in the pelvic organs.

Until recently, the collective term "nervousness" was used in the medical diagnosis of dysmenorrhea. This precept still exists in the attitude of physical education toward dysmenorrhea. What was formerly called "nervousness" is often a true imbalance of the organic autonomic (sympathetic) nerve system. This may first lead to disturbed function, but later to tangible, structural damage in the machine. In the uterus, the *structural* damage is usually minor and negligible, but the *functional* damage may be the cause of serious pain. It is further noted that in the dysmenorrheic young girl, a chemical stimulus for pain is provided by the unbalanced chemistry of her maturing hormonal system. However, the strength of her reaction depends not only on the stimulus but also on her physical constitution.

In dysmenorrheic disturbance, the inherited physical constitution influences 3 factors: (1) the hormonal function and thereby the chemical stimulus; (2) the

The author speculates on the *modus operandi* of the relief of menstrual pain with curare. The drug may improve the circulation to the uterine muscles by its relaxing action on all skeletal musculature. Bickers believes that the pain of dysmenorrhea is comparable with that of angina pectoris and other painful muscular contractions caused by insufficient oxygenation of the contracting muscles.

(The old South American arrow poison seems to be coming into its own in the field of therapeutics. It enjoys rather wide vogue as a relaxant during anesthesia, and now it is suggested for dysmenorrhea. The disadvantages enumerated by the author herself seem real, especially that the drug must be given parenterally. I somehow feel no particular urge to try this method of treatment.—Ed.)

## MENSTRUAL DYSFUNCTIONS; ABNORMAL UTERINE BLEEDING

S. CHARLES FREED

West. J. Surg., 54: 45-49, 1946

Abnormal uterine bleeding, like amenorrhea, may be a sign of systemic disease, endocrine disorder, or the result of ovarian dysfunction.

*Menorrhagia:* This occurs cyclically as in normal menstrual bleeding, except that the flow is profuse and often prolonged. The cause is often obscure, although one must not overlook a bleeding dyscrasia with a faulty clotting mechanism. Hypothyroidism often results in excessive menstrual flow and psychic factors may also play a causative part. The fact that curettage alone often corrects the condition suggests at times that the endometrium is refractory to the action of progesterone.

Treatment may be accomplished by a number of technics. Curettage is sometimes effective. Estrogens administered in fairly large doses before the onset of ovulation may suppress or decrease the flow. Androgen therapy has been most helpful, especially where it is essential to stop the bleeding to prevent exsanguination. The danger of virilism when administering androgen therapy exists if the dosage exceeds 400 mg. per month. Naturally, thyroid substance is indicated where there is a thyroid deficiency.

*Poly-menorrhea:* This term refers to the occurrence of menstruation at intervals of 20 days or less. The condition has been claimed to result from an early regression of the corpus luteum, so that its life is decreased from 14 days to about 7. It may also occur in disturbances such as under-nutrition, psychic disorders and infectious diseases. Treatment is not urgent but estrogens may be used in doses of  $\frac{1}{2}$  to one mg. per day, which will restore a normal period, especially in older women.

*Intermenstrual bleeding:* This often occurs at the time of ovulation and may be associated with *mittelschmerz*. When the bleeding is scanty, it may be due to

whole patient, body and mind—as in dysmenorrhea. The author very properly emphasizes not only the harmlessness but the actual value of physical exercise, not only for its actual physical benefits, but because it is likely to develop a healthier psychological attitude.

These comments should not be construed as meaning that the cause of primary dysmenorrhea is always psychogenic, a viewpoint urged by some gynecologists, but not subscribed to by me. However, in a condition so obviously subjective as dysmenorrhea, the psychological factor is quite sure to intertwine itself quite inseparably, so that it should never be overlooked. As to the actual cause of the menstrual pain in so many thousands of anatomically normal girls and young women, we are still in the dark, and it is probable that the mechanism is a protean one. It would be hard for the author of this paper to prove that in this disorder "a chemical stimulus for pain is provided by the unbalanced chemistry of her maturing hormonal system." The endocrine vogue in the treatment of dysmenorrhea had its inception when it was found that the two ovarian hormones play an important rôle in the contractility of the uterine musculature, but many years of laboratory investigation have not yet brought about a consensus as to the exact nature of this hormonal control, certainly in so far as progesterone is concerned.

Nor can it be concluded that heightened and colicky muscular contractility is the cause of the menstrual pain, though most of our methods of treatment are directed by this assumption. It is possible that vascular rather than muscular wall spasm is the important factor, but this likewise cannot be proved. Fortunately, most cases of dysmenorrhea are of moderate degree and the sensible plan of treatment, in addition to reassurance, education, psychotherapy and general measures, including exercise, is the administration of the few doses of simple analgesics required to make the patient's lot tolerable. If the pain lasts only a day or so, as is so commonly the case, this simple plan is preferable to long courses of "shots" which are likely to keep the patient's mind centered on her trouble. For the very severe cases, involving severe pain for many days, more active measures, even including presacral sympathectomy, may be necessary. But a properly conservative gynecologist will find this necessary in only a small proportion of the dysmenorrhea cases which he sees.—Ed.)

## USE OF CURARE TO RELIEVE DYSMENORRHEA

FLORENCE JOHNSTON

Am. J. Obst. & Gynec., 51: 569-570, 1946

The author reports the results obtained with the administration of curare to relieve dysmenorrhea in a total of 49 women in 73 menstrual periods. Good results were obtained in 50 per cent of the cases; by good results is meant that the patients were able to return to work within 20 to 30 minutes and to continue their normal activities with little or no discomfort. Another group had temporary or partial relief of pain and about one-third of the patients had no relief or such short relief as to make the use of curare impractical.

The necessity for parenteral administration of curare limits its usefulness. Within one minute after intravenous injection of curare the patient experiences heaviness of the eyelids and often diplopia, or fuzzy vision. These effects pass in 5 to 10 minutes. The relief is experienced within 2 to 15 minutes after the intravenous injection of 50 to 100 mg. of curare.

nate signify ovarian failure with varying degrees of rapidity. The typical climacteric changes may be separated roughly into 2 categories: organic changes in the tissues, and functional disturbances which include the psychic and circulatory disturbances.

*Organic changes:* These changes are manifested over the entire body but are most marked in those organs which respond to the greatest degree to the stimulus of the ovarian hormones. Also, changes are noted in other endocrine glands which bear a reciprocal relationship to the ovaries. The anterior hypophysis is altered in function, its cells indicating that the gonadotropic secreting cells become hyperactive. Whether the thyroid gland is altered during the climacteric has been speculated, since the symptoms of the patient in the climacteric often simulate those of the thyrotoxic individual. By administering therapeutic doses of estrogen a differential diagnosis may be obtained with dramatic relief of the typical menopausal symptoms, thus ruling out thyrotoxicosis.

There may be a functional disturbance of the adrenal cortex due to the imbalance between the estrogen of the ovary and the androgen of the adrenal cortex. There is a relatively high incidence of carbohydrate metabolism disturbances during the climacteric which may be of adrenal origin.

It is possible that the development of diabetes, arthritis or obesity during the menopause is not the result of a direct relationship between the ovarian failure and these organ changes, but that the menopause predisposes to the development of these conditions, primarily through intensifying certain underlying tendencies.

The most marked changes are those which involve the regression in the accessory sex organs, namely, the breasts, uterus and vagina. The breasts undergo atrophy as well as the uterus, and even certain pathological structures of the uterus such as fibroids and myomas may regress. However, some women show a fairly well developed endometrium and some a certain degree of hyperplasia. In most cases there is a marked atrophy of the lining of the vagina which can readily be seen in the vaginal smear. However, in a considerable number of women a fairly well developed mucosa is seen, making the use of the vaginal smear unreliable in certain cases.

Changes in the cardiovascular system may result in typical hot and cold flushes, palpitation and headache. Changes in the electrocardiogram can be reversed upon substitution therapy. If the cardiovascular symptoms persist for a long time without treatment permanent damage to the heart and blood vessels may develop.

*Functional changes:* Menopausal patients may become nervous, irritable, emotionally unstable, and tensions of all types may arise. The extreme degree of psychic disturbances occurring at this time is so-called involutional melancholia. In the treatment of these psychosomatic disorders, probably one of the first steps is the restoration of the proper threshold level by adequate estrogen substitution therapy.

*Treatment:* The 3 main agents used in treatment are general medical therapy, psychotherapy and hormonotherapy and the 3 are intertwined and inseparable. In medical treatment sedation with barbiturates is often adequate. Hyperten-

either of 2 factors: (1) Ovulation may result in the rupture of some peri-follicular capillaries with the leakage of a small amount of blood down the tubes. (2) It may result from engorgement of the uterus with an oozing of blood through the endometrium. More profuse bleeding must be considered due to a different mechanism. It is not unlikely that the dip of the estrogen level following the peak at ovulation goes past the bleeding threshold, so that bleeding of the endometrium resembles that of a menstrual flow. In practically all cases small doses of most estrogens by mouth or injection for 2 or 3 weeks will eliminate the intermenstrual flow.

*Metrorrhagia:* Prolonged bleeding from the uterus is one of the most troublesome of ovarian dysfunctions. There is a greater incidence of hyperplasia in such cases and the condition is encountered more commonly in older women and in those who have had children. The causes may be associated with certain systemic disorders or involving other glands. Malnutrition and a decreased vitamin B intake may induce such changes. Certain tumors of the ovary in which hyperplasia is found, such as granulosa cell tumor, may be responsible. Insufficient contraction of the muscles of the uterine wall upon the spiral arteries may result in continuous bleeding. Uterine biopsy is essential for diagnosis and vaginal smears may be useful.

In the younger groups, spontaneous correction may occur in about 50 per cent of the cases: When there is extensive hemorrhage, calcium, ergot, posterior pituitary and snake venom may help in the immediate control of the bleeding. Thyroid and vitamin B administration may prove dramatic in cases of deficiency of these substances. Endocrine therapy is of great value with estrogen therapy the treatment of choice. Androgen therapy should be reserved for a younger patient when there is hesitation to administer large amounts of estrogen.

(This is a brief review of the various forms of abnormal functional bleeding, with suggestions as to some of the innumerable plans of treatment. Others could have been mentioned by the author. For functional menorrhagia, large doses of estrogen, usually in some such oral form as diethylstilbestrol, often bring about rather prompt temporary relief, so that they may obviate the necessity of curettage. As for testosterone, the mention of which makes some endocrinologists froth at the mouth, I agree that it is often justified and beneficial, though I would put the upper safe limit at 200 rather than 400 mg. monthly, in so far as virilism symptoms are concerned. For lengthening the cycle, in the occasional cases of polymenorrhea in which this might seem desirable, I have found progesterone more helpful than estrogen.—Ed.)

## MENSTRUAL DYSFUNCTIONS; THE CLIMACTERIC

S. CHARLES FREED

West. J. Surg., 54: 103-109, 1946

The objective features of the climacteric are chiefly those of alterations in uterine bleeding. All of the different patterns in which the menses may termi-

necrosin-like extracts into intraocular endometrial transplants causes a 4-hour constriction of the basal part of the coiled arteries. It is therefore probable that the vasoconstriction which begins 4 to 24 hours before the onset of bleeding, and persists throughout it, is controlled by a necrosin-like substance. Variations in the concentration of this substance are probably responsible for the relaxation of the individual coiled arteries before and during individual hemorrhages; also, for the subsequent constriction of the appropriate coiled arteries and the consequent termination of hemorrhage from them.

(It will be recalled that it was Markce who demonstrated the important rôle of the endometrial vessels, especially the spiral arterioles, in the mechanism of the menstrual cycle, certainly one of the most outstanding contributions in this field. In this paper he is concerned especially with the part which may be played by the necrosin-like substance which he describes in the mechanism of menstrual bleeding. While there is still much to learn about the subject, more and more investigators appear to be stressing the importance of some toxic protein substance as an immediate factor in the cause of menstrual bleeding.—Ed.)

## DELAYED OVULATION IN THE MACAQUE MONKEY

I. ROSSMAN AND G. W. BARTELMEZ

Anat. Rec., 94: 411, 1946

Ovulation in the macaque usually occurs sometime between the end of the first and the beginning of the third week after the onset of the last menstrual period. In a colony of 30 normal mature animals four cases of "delayed" ovulation were observed in the course of a breeding season during which frequent rectal palpations were made by Hartman's method. Normal ovulation was detected on the 29th, 29th to 30th, 30th and 36th to 37th days, respectively, after menstruation. The findings indicate unusually long periods of inactivity postmenstrually. Histologic study of uterus and both ovaries in each case verified the palpation data. Only histologic evidence of such delay was available in five additional cases culled from the Hartman, Corner, VanDyke and Chicago Collections of macaques. There are reasons for believing that long postmenstrual phases may occur in women. They would account for many of the cases that have been cited to prove that ovulation may occur at any time during the cycle, even during the catamenia itself.

(Whereas formerly there was much difference of opinion as to whether, in abnormally long or abnormally short cycles, it is the pre-ovulatory or post-ovulatory phase which is the variable, the evidence now seems quite complete that it is the pre-ovulatory phase which is subject to these variations, while the corpus luteum phase is of rather fixed duration. The bearing of this fact on such questions as the so-called safe period is obvious, as also on the opposite question of optimum time for fertilization in the case of women anxious to conceive. Moreover, as the authors point out, such observations as they report of delayed ovulation explain the otherwise confusing instances reported of ovulation occurring much later in the cycle than the accepted ovulation phase.—Ed.)

sion and its complications and diabetes require orthodox medical treatment. Psychological treatment in the menopause cannot be overestimated; it may include assurance, understanding and the use of powerful suggestion. In severe cases a specialized psychotherapy may be required.

The author discusses the endocrine therapy of the menopause with particular reference to the estrogens which are the fundamental endocrine agents in menopausal relief. Dosage and mode of administration depend upon the individual patient, the severity of symptoms and the temperament of the physician. If toxic results occur below the therapeutic level of the estrogen dose it is well to abandon oral therapy and resort to injections of the more slowly absorbed estrogens. Other complications such as painful breasts and uterine bleeding may be relieved either by temporary cessation of estrogen therapy or by the administration of androgens, such as testosterone propionate.

(A satisfactory review of an important subject. Many sins of treatment are still committed in this field, especially in the too ready resort to estrogen therapy, often for symptoms not genuinely menopausal. The potency of oral stilbestrol therapy has led to indiscriminate employment of this drug, with postmenopausal recurrence of bleeding which may be disturbing to both patient and doctor, and there may be concern as to the possibility of adenocarcinoma. Much has been written on this subject, but the evil is still widely prevalent. Neither this drug nor any other estrogen should be given for long continuous periods or in too large dosage, but only when and if the typical vasomotor symptoms are very troublesome.

The term involutional melancholia is still used rather loosely. Some seem to apply it to the mild depressive symptoms occasionally seen at the menopause, and in such cases estrogen therapy may be helpful as a part of the treatment. More properly the term is applied by psychiatrists to a genuine psychopathy of the middle age period, not causally related to the menopause, and not likely to be influenced by estrogen therapy, except in so far as any associated vasomotor symptoms are concerned.—Ed.)

## THE MORPHOLOGICAL BASIS FOR MENSTRUAL BLEEDING

J. E. MARKEE

Anat. Rec., 94: 481, 1946

In the rhesus monkey growth of intraocular endometrial transplants is preceded by an increased blood supply of the endometrium. Conversely, endometrial regression is preceded by a decreased blood supply following either complete or partial withdrawal of the ovarian hormones or affront to the nervous system. The reduction in blood supply involves both a slowed flow and a relative reduction in the amount of oxyhemoglobin. The above vascular changes apparently shift the fluid balance away from the stroma towards the blood stream and thus contribute to regression. The rapid decrease in thickness of the endometrium is followed by knotting and buckling of the coiled arteries and consequent stasis in them. This stasis apparently causes the premenstrual necrosis and during the necrosis a substance resembling necrosin is probably produced. The injection of

## VULVA AND VAGINA

### LEUKOPLAKIC VULVITIS AND ITS RELATIONSHIP TO THE DEVELOPMENT OF CARCINOMA OF THE VULVA

E. GARLAND HERNDON, JR.

J. Bowman Gray School Med., 4: 35-45, 1946

Leukoplakic vulvitis occurs very infrequently and is rarely seen in general practice. The incidence of the disease in one series of 9682 gynecological patients was 0.24 per cent. Leukoplakic vulvitis is a chronic inflammatory process characterized by agonizing pruritis of the vulva which becomes unbearable if allowed to progress. It is felt by most authors that leukoplakia of the vulva is definitely related to ovarian function and is distinctly a disease of the menopausal or post-menopausal years. Taussig believes that in some women in these age groups a special disturbance of ovarian secretions causes a complete disappearance of the elastic tissue in the upper layers of the vulvar skin, leading to greater friability and minute breaks of the skin through which bacteria gain entrance, with the resulting exudate causing pruritis. The disease is progressive and does not tend to regress spontaneously, although there may be periods of quiescence.

The clinical manifestations include intense pruritis and burning after urination. Pain on defecation is present if the anal region is involved. A large number of cases have a pronounced vaginal discharge and in many cases with kraurosis, dyspareunia is marked. A certain number of patients have joint pains.

The disease is a definite precursor of cancer of the vulva in 50 per cent of the cases. Over a certain period of time Taussig has seen 40 cases of leukoplakic vulvitis without cancer and 39 cases with cancer. Other investigators have reported similar findings. Cancer may develop at any of the 3 stages of leukoplakic vulvitis, but it is most frequent and most malignant when it originates in the 2nd stage, that of epithelial hypertrophy. Next to cancer of the uterine body vulvar cancer is the most benign type found in the female genital organs. Approximately 50 per cent can be prevented and, after they have developed, about 60 per cent can be permanently cured.

Surgical removal of the involved tissue is the only safe, logical and effective therapy in alleviating the symptoms and arresting the progress of leukoplakic vulvitis. Vulvectomy is further justified as a prophylactic measure against cancer of the vulva. Postoperatively the patients should be followed closely for the possibility of a recurrence of the leukoplakic vulvitis or recurrence of carcinoma if it was present at the time of operation.

Three case reports are presented and discussed by the author.

(The author of this satisfactory review appears inclined to the endocrine explanation of the etiology of leukoplakia, although the evidence along this line is rather slim, and estro-

## A TEST FOR DETERMINING THE APPROXIMATE TIME OF OVULATION IN WOMEN AND IN MONKEYS

E. J. FARRIS

Anat. Rec., 94: 460-461, 1946

A new test for detecting a reaction associated with ovulation was made upon a series of women and *Macacus rhesus* monkeys. The test is based on the observation that the urine collected at about ovulation time produces hyperemia of the ovaries of an immature rat, when administered to the rat subcutaneously. It is postulated that a sequence of positive reactions indicates that ovulation is impending. The resulting observations in 100 women indicate whether and when ovulation is occurring.

Predictions were confirmed by eighteen pregnancies. Assays of the urine show gonadotrophin when the reaction is positive. A 16-mm follicle, as predicted, was observed in an ovary in one case at surgery.

In all of the seven monkeys in which the test was positive, ovulation was confirmed at laparotomy by Dr. George W. Corner. In all four animals in which the reactions were absent, laparotomy in one case and bimanual examination in three others failed to show ovulation.

(This test will of course need confirmation, but at the best it would not seem as simple as other reliable tests of ovulation already available, such as endometrial biopsy or basal temperature records.—Ed.)

necrosis and infection have developed it is easy to see how it might be mistaken for an inflammatory lesion. By many this form of carcinoma is looked upon as only a variety of vulvar carcinoma, as indeed it is, and its treatment is along the same lines. In general, and subject to perhaps some individual exceptions, total vulvectomy with excision of not only the inguinal but also the deeper pelvic glands surrounding the iliac vessels, would be the procedure of choice, followed by postoperation roentgen therapy.—Ed.)

## STUDIES OF THE ORIGIN AND TREATMENT OF RECURRENT TRICHOMONAS VAGINITIS

EDWARD ALLEN AND STUYVESANT BUTLER

Am. J. Obst. & Gynec., 51: 387-394, 1946

Recurrent trichomonas vaginitis remains one of the most difficult therapeutic problems in pelvic infection. Thus far, little positive evidence has been presented as to the manner in which the organism first gains admission to the body, and the method of extension to other organs. The authors present a brief résumé of important literature dealing with species differentiation of *Trichomonas vaginitis*. The literature reveals increasing evidence differentiating vaginal and intestinal species of trichomonads.

In an attempt to rule out the intestinal tract as a possible source of infection or reinfection of the vagina with *Trichomonas*, a series of 39 treatment-resistant cases were studied by proctoscopic examination. No trichomonads were found in the bowel cultures.

Certain visual changes were observed in the rectal mucous membrane of a large percentage of these patients. These changes were seen in an area on the anterior wall approximately 7 cm. above the anus, contiguous to the posterior fornix of the vagina. The changes consisted of redness, swelling, dilated veins, granulation, or pinpoint ulceration. The authors cannot be sure whether or not there is any relationship between the lesions in the rectal mucous membrane and the vaginal infestation with *T. vaginalis*; however, they occurred with such regularity in the same area of the rectum as to appear more than merely coincidental.

Six other cases which had positive stool cultures for *T. hominis* were examined vaginally. In no case was *T. vaginalis* found in the vaginal secretion. One case with intestinal trichomonads was followed for 10 months, but the vaginal smear remained negative.

The authors have been unable to demonstrate any ascension of the trichomonads above the external os of the cervix. Immediate examination of surgical specimens taken from the uterine canal, tubes, ovarian cysts, pelvic and ovarian abscesses and amniotic fluid of 28 patients with active *Trichomonas vaginitis* revealed no organisms in direct smear or culture.

The plan of treatment for this series has consisted mainly of the following routine: nightly insertion of a tablet of lactobacilli; a morning cleansing douche

genic therapy has been notoriously unsuccessful. The general feeling is not that 50 per cent of leukoplakia cases become malignant, but that in 50 per cent of vulvar carcinomas leukoplakia has been a precursor, which is a little different. If surgical treatment embraces only vulvectomy and inguinal adenectomy, as it formerly did, the proportion of permanent cures would scarcely exceed 10 per cent or so. The very rich lymphatic drainage of the vulva, extending not only to the inguinal but also to the deeper glands of the pelvis along the iliac vessels, necessitates far more extensive operations of the Basset type. With such extensive surgical procedures a far greater salvage, approximately 50 per cent, has been reported by Taussig and others.—Ed.)

## CARCINOMA OF BARTHOLIN'S GLAND

LUCIEN A. LEDOUX

New Orleans M. & S. J., 98: 454-456, 1946

Carcinoma of Bartholin's gland is a rare occurrence. It grows slowly, is self-contained in its early stages and metastasizes very slowly. The etiology and age incidence are the same as in other forms of genital malignancy. The histopathology is about equally divided between the squamous cell type and adenocarcinoma. Trauma of the indurated vaginal mucosa probably accounts for the co-existence of an abscess and a malignant picture.

All cases of Bartholin cyst and abscess should be carefully scrutinized for possible malignancy. The treatment consists of a careful dissection and excision of the gland and adjacent tissues with immediate irradiation.

The author presents a case of a woman, aged 52 years, who was first seen because of a running sore which began about one month prior to examination as a swelling of a gland on the right side of the vulva. Examination of the external genitalia revealed what appeared to be a ruptured Bartholin gland abscess on the right side. A small amount of pus exuded from the opening and the smear showed *B. coli*.

A total excision of the gland was done and the pathological diagnosis confirmed the suspicion of malignancy. Even though the tumor appeared self-contained, the operation included a complete dissection of all fat tissue surrounding the gland down to the fossa, removal of the affected vaginal tissue and plastic repair. During her hospital stay radium was applied externally to the affected area for 350 mgm. hours. The pathologic diagnosis was squamous cell carcinoma—Grade III.

About one year later there was some evidence of redness and cracking of the tissues at the site of the old lesion and 150 mgm. hours of radium were given as a precautionary measure. More than 7 years have elapsed since her operation and she feels well and has remained well.

(As the author states, primary carcinoma of Bartholin's gland is a rare disease, adenocarcinoma being probably more frequent than epidermoid carcinoma. In the earlier stages it presents as a hard, nodular mass in the usual location of the gland. When secondary

Grossly one may see an excess of white or yellowish discharge between the labial folds, acute to subacute redness of the inner aspect of the labia and hymen and brownish excoriation of the perineum. There may be redness and edema of the vaginal mucosa with an excess of milky to yellowish leukorrhea and a collection of vaginal secretion in the posterior fornix. There may be "flea-bitten-like areas" on the anterior wall and cervix with lesions around the external os and areas that bleed from the slightest manipulation.

In order to complete the diagnosis, microscopic examination must be made of material which is gently scraped from the posterior wall of the cervix and vaginal walls. Typical clear motile flagellates are observed moving among the debris in the secretion. In normal saline, at room temperature, the trichomonads multiply and live for 4 to 24 hours.

In the author's 12 years of studying this condition, many therapeutic measures have been used. The most efficient results were obtained in 400 patients with *Trichomonas vaginalis* by the use of floroquin. Two to 8 tablets were inserted in the vagina with a cotton plug at the introitus and the patient inserted one or 2 tablets twice a day for 12 days with no douching. At the end of 12 days, the patient took a douche containing 10 tablespoons of vinegar twice a day for at least 3 months. Most of the patients in this series had an associated cervical ectropion. This was treated by conization (preferable), cauterization or coagulation followed by a cotton plug in the coned area and a vaginal pack of floroquin tablets and cotton. This pack was removed and a new one inserted twice a week for 3 weeks. At the end of 3 weeks, the patient followed the douche regime described above. If trichomonas recurred, the patient started vinegar douches 4 to 6 times a day for one week to destroy the new infection before it became established in the vagina. 2 figures.

(The author has evidently repeated the rather heroic experiments of Trussell and Plass (Am. J. Obst. & Gynec., 40: 833, 1940) of direct inoculation into the vaginas of normal women of trichomonas, with the production of typical trichomonas vaginitis, just as the above authors did. The chief difference is that Trussell and Plass employed pure cultures of trichomonas rather than mixed cultures of the parasites and vaginal bacteria, as Karnaky did. From this standpoint, the work of the Iowa investigators seems even more conclusive than that of Karnaky in establishing the causative role of the trichomonas itself. The treatment recommended, like a great many others, is satisfactory as to immediate improvement in the vaginal condition, but recurrences may occur with this as with other methods. Incidentally, a patient who has to take 4 to 6 douches a day is likely to be a busy little woman while working for her cure.—E.)

## "LYMPHANGIOMA OF THE VAGINA"

PIETRO DE NICOLA (*From Bologna, Italy*)

Pathologica, 38: 26-32, 1946

The writer reports a case of vaginal lymphangioma (although an origin from the recto-vaginal septum could not be entirely ruled out), other cases of which

consisting of 1 dram of lactic acid to 2 quarts of warm water, followed by the instillation of one applicator full of jelly for daytime use. Of 166 patients, 62 were cured by the use of jelly and douches alone. The authors believe that the addition of lactobacilli tablets will materially increase the number of permanent cures.

In cases of recurrence, an immediate search is begun for secondary foci of infection. The bladder has been a demonstrable focus in 21 per cent of 234 cases. If urinary tract investigation bore no fruit, the male partner was examined. In several instances, motile trichomonads were found in the prostatic fluid. 2 figures.

(While it has been rather generally assumed that the intestine is the probable source of infection in trichomonas vaginitis, the present study provides good evidence against this theory, so that the problem remains, if anything, more baffling than ever.—Ed.)

## TRICHOMONIASIS; A TWELVE YEAR STUDY

KARL JOHN KARNAKY

West. J. Surg., 54: 61-64, 1946

This paper deals with the incidence, pathogenicity, diagnosis and treatment of *Trichomonas vaginalis*.

The incidence of trichomonas varies according to the training the physician has had in looking for them in a fresh, unstained vaginal smear and to the race of the patient. Others have reported incidences varying from about 13 per cent to 66 per cent, the latter incidence being found in a group of prostitutes. In 2173 consecutive repeated fresh smears on the same group of about 700 patients, the author found 23.42 per cent positive by fresh smear, 30.57 per cent diagnosed clinically, 21 per cent diagnosed clinically and also by fresh smear and 0.243 per cent diagnosed, not clinically, but by a fresh smear. The patients in the last group harbor the organism.

The author has inoculated vaginas free of *Trichomonas vaginalis* with mixed cultures of bacteria and trichomonads and produced all signs and symptoms of *Trichomonas vaginalis*. Bacterial cultures from trichomonal infested vaginas were inoculated into a large series of vaginas free of trichomonads. No signs or symptoms of *Trichomonas vaginalis* were produced.

The relationship of the bacterial flora, vaginal pH, glycogen in vaginal secretion and epithelium and Döderlein bacilli appears to play an important part in trichomonal infections. It was observed that at pH's below 5.0, trichomonads in mixed bacterial flora died. No trichomonads were found in vaginas made acid, below 5.0.

In the diagnosis of *Trichomonas vaginalis*, one finds a history of a profuse thin leukorrhea which causes a pruritus vulvae with scalding of the external genitalia.

variety seems to be the larvae belonging to the *Cochliomyia hominivorax* or *americana* variety.

The flies are attracted to the external genitals by the odor secondary to the discharge of wounds or lack of cleanliness, especially during menstruation, in women who expose the genitalia to the insects by not wearing proper underclothes. The flies deposit their eggs in the vulva, from which grow the larvae responsible for the lesions which they produce by destroying the tissues. Deep large ulcerations are thus formed. These are very sensitive and present an offensive sero-hemorrhagic discharge. Within a short period of time various fistulas are produced aside from the initial ulceration, in which the larvae can usually be found in large numbers.

The evolution of the disease is very rapid, since the larvae ordinarily leave the patient 8 to 10 days later. However, the latter has to seek treatment before this happens, because of the severity of the pain.

The prognosis is good. Whatever form of treatment is used, this should be preceded by thorough cleansing and drying of the infected region.

Case Report: A 44 year old patient with positive Wassermann developed deep and extensive ulceration on her right labium majus, where a small wound of surgical nature had previously been present. One hundred and sixteen larvae were removed from the entire lesion and proved to be of the *Cochliomyia hominivorax* variety.

Treatment was directed against syphilis, with bismuth injections. In addition, specific therapy for the myiasis consisted of intravenous injections of mercury oxycyanuret (Prado Moreira's method) every other day, and daily local applications of iodoformized ether with xylol (Stabiles's method). The results were very good, and complete healing of the lesions occurred.

(I am sure that it will surprise most of our American readers that the larvae of the common fly can become parasitic in the tissues of the human vulva, and that such extensive lesions may be produced. The author of this report, a highly trained gynecologist of São Paulo now in this country, and the author of an excellent monograph on leucoplakia of the vulva, tells me that a number of instances of this type of vulvar larval infestation have been reported in South America.—Ed.)

are yet unknown in the literature. This case is included within the group of lymphangiomas of the female genital apparatus, i.e., ovaries, tubes, uterus and vulva. Attention is focalized on its macroscopic and microscopic features in comparison with other vaginal lesions; some hypotheses regarding its histogenesis are suggested and, finally, the therapeutic problem is brought forth.

Case report: 42-year-old patient who had seven years ago noticed a growth the size of a walnut, asymptomatic, situated on the posterior vaginal wall. Three years later, after having had severe hemorrhages preceded by a period of amenorrhea, the tumor started growing rapidly. Pelvic examination revealed a left ovarian cyst and a large protuberance of the posterior vaginal wall, due to the presence of an elongated mass the size of a fist, carneous in consistency, fixed and painless. Through rectal examination, it seemed that the rectal wall was not involved.

Biopsies showed the tumor to be a lymphangioma of the simple type, according to Leccne's classification. The histologic picture was essentially that of several cavities presenting the proper structure of lymphatic vessels and lacunae, separated by strands of connective tissue. Within the latter there were numerous lumina lined by endothelial elements and surrounded by delicate elastic filaments. In some areas deposits of hemosiderin could be found and, at deeper levels, muscle fibers. By means of silver impregnation, the supporting tissue was seen to be made up of a delicate reticular network. The patient was treated with radium, but the results are not reported.

(This growth, according to the histological description, appears to have been a genuine lymphangioma, a very rare tumor of the vagina. Since the rectal wall was not involved, one wonders why it could not have been excised, which would seem to have been a better plan than radiotherapy. Since there was apparently considerable endothelial overgrowth, perhaps the tumor is more properly to be classified as a lymphangioendothelioma, with at least a certain degree of malignancy.—Ed.)

## MYIASIS OF THE VULVA

OCTAVIANO ALVES DE LIMA, JR.

Rev. de ginec. e d'obst., 39: no. 2, 1945

In this paper the writer presents a general review of the literature concerning the rare occurrence of myiasis in the vulva, describes its clinical picture and presents a case of his own which he had the opportunity of studying.

Myiasis refers to the lesions produced in men and mammals as a result of the parasitism of the larvae of flies. They are quite frequent in various parts of the body (ears, nose, etc.), but, on the other hand, their occurrence in the vulva constitutes a very rare condition.

In the Western hemisphere, the more common agent of myiasis of the cavity

the woman's, but it is the physician's responsibility to teach her the correct facts about genital health. It is useful to spread information that discharges and abnormal bleedings are the first symptoms of cancer of the cervix, but it is far more important to emphasize that the time to detect the disease is before it causes symptoms, which is possible only by routine pelvic examinations. It should also be taught that menopause means the cessation of monthly bleeding and that discharges and irregular bleeding are neither physiologic nor to be tolerated during the climacteric.

Some method must be used to impress upon the patient with the disease the fact that her life depends upon obedience to her physician's instructions and advice. Several patients in this series whose malignancy was diagnosed refused to receive treatment. If it is necessary to scare patients to death in order to frighten them into life, then that must be done. Whatever is necessary to induce them to submit to diagnosis and treatment would be justified; their lives are at stake. However, the patient is not likely to be impressed with the urgency of her disease until physicians begin to comprehend its urgency. It is emphasized that *all* physicians, and not merely gynecologists, must share this responsibility.

In general, it may be said that a woman who is examined yearly from the ages of 25 to 35 years, and twice yearly thereafter, has taken adequate prophylactic measures against the development of cervical cancer. Attention to the cervix after childbirth would also be helpful.

The economic and social factors implicit in carcinoma of the cervix are discussed, and attention is called to the tragic plight of women who are discharged from the hospital because treatment is useless and the facilities of the institution must be saved for those who can be helped.

(Comment has already been made, in the preceding number of the Survey (p. 402), on the courage and honesty of the authors in their papers, of which this is the third, devoted to a pitiless analysis of the past derelictions and inadequacies of treatment in the large series of cases coming under treatment in their clinic. It is quite certain, from the intelligent viewpoint of the authors, that the present day management of cases in the same clinic shines by contrast.

I agree with the authors that our greatest hope for improvement in results must be in getting an increasing proportion of our cases in the early favorable stages of the disease. The authors rightly call attention to the importance of education of women. In spite of all the propaganda of the past twenty-five years or so, there are still many women who delay because of the entire absence of pain, or because they have the foolish idea that excessive or irregular bleeding is natural at the change of life. On the other hand, the skirts of our own profession are far from clean. It is particularly tragic to encounter cases in which the woman herself has been alert and intelligent enough to seek periodic examination, or has sought advice because of abnormal bleeding, but has been dismissed by her doctor with a perfunctory examination, or no examination at all, and perhaps the advice to go home and forget about it. Only the most meticulous examination of the cervix, not only by palpation but by minute inspection in the best possible light, can be considered conscientious. And the doctor must train himself to learn the characteristics of very early lesions, and he must follow through relentlessly with biopsy if there is the slightest doubt. For these differentiations he will usually wish to refer the patient to the gynecologist trained in such technical procedures, especially since they involve pathological differentiation studies. In this group of cases, the patient must be put to a little trouble, and the doctor must sweat a

## THE UTERUS

### CARCINOMA OF THE CERVIX; AN ATTEMPTED FOLLOW-UP STUDY OF 500 CASES. III. THE ROAD TO IMPROVEMENT IN RESULTS

PETER GRAFFAGNINO AND ELIZABETH M. McFETRIDGE

New Orleans M. & S. J., 98: 399-405, 1946

In 2 preceding papers based on an attempted follow-up of 500 cases of carcinoma of the cervix certain statistical data were presented and certain therapeutic and diagnostic considerations were presented. The most important statistical fact was that of the 397 patients whom it was possible to follow-up, 358 are known to be dead and 39 are known to be alive for periods varying from 7 to 12 years after treatment. The most important therapeutic consideration was that during the years of this study the radio-therapeutic facilities of the hospital were utterly inadequate, but that the best use was not always made of such facilities as were available. The most important diagnostic consideration was that at least 27 patients who consulted physicians outside the hospital when first symptoms developed received egregiously wrong advice, while the hospital staff was not always free from diagnostic errors.

The purpose of this, the third paper in the series, is to analyze the end-results in these 500 cases from the standpoint of the patient's responsibility for her own fate, and to consider how it would be possible to improve the results in this disease by the application of certain educational and prophylactic measures.

The solution of the problem of carcinoma of the cervix is not therapeutic improvement, important as such improvement would be, but rather diagnostic improvement, which does not mean seeing the patient immediately after the onset of symptoms. A number of patients in this series appeared at the hospital within 2 or 3 weeks, and sometimes within a few days, after their first symptoms, which were usually in the form of hemorrhage, yet some of them had advanced, incurable stage 4 disease. The idea of constant, continuing attention to the pelvic organs *in the absence of symptoms* must be presented to every woman and kept before every physician.

A vaginal discharge, with or without spotting, is the most frequent symptom of carcinoma of the cervix and, judging by this series, is also the least heeded. Irregularities of menstruation, particularly at the time of the menopause, was next in point of frequency. Pain and hemorrhage were the symptoms which brought the patients most promptly to the hospital and it may be significant that these were the presenting symptoms in 11 of the 39 patients known still to be alive.

There must be a different educational approach if the present results are the best that can be achieved by the efforts and money spent on educating the public during the past 2 decades. The ultimate responsibility for her own fate may be

In the present study, the authors were unable to show that porphyrins are related to malignancy. However, this does not mean that the porphyrin hypothesis has been disproved, for the proof of a definite relation to malignancy may be a very difficult endeavor. 1 figure.

(This is a rather difficult paper to read and digest. Perhaps one should not feel too badly about this, since the studies reported are of rather negative and hypothetical nature, in spite of the rather interesting color reaction described.—Ed.)

## TREATMENT OF CHRONIC CERVICITIS

KARL JOHN KARNAKY

Clin. Med., 53: 47-50, 1946

Cervicitis may be acute or chronic, mild or severe, productive or non-productive of leukorrhea. The most common symptom or sign is a thick sticky leukorrhea which does not itch or burn. If the cervicitis is due to *Monilia albicans* or *Trichomonas vaginalis*, there is a thin itchy leukorrhea.

In a young girl near puberty, cervicitis is usually due to a previously dormant congenital ectropion which, under the influence of estrogen, produces mucus. Cervicitis during married life may be due to gonorrhea but is more often due to pyogenic microorganisms or an infected laceration of the cervix following labor. In women past the menopause senile changes, *Trichomonas vaginalis* and cancer cause cervicitis.

Acute cervicitis clears up spontaneously in 2 to 4 weeks if sulfadiazine is given.

Chronic cervicitis accounted for 94 per cent of the cervicitis cases seen in the author's clinic. Chronic exocervicitis is usually seen in cases of syphilis, leptothrix in *Monilia*, *Trichomonas*, non-specific and mild gonorrheal infections. Chronic exocervicitis (ectropion) is usually seen 6 weeks to 6 months after childbirth. Gonorrheal cervicitis first appears as an acute cherry red lesion surrounding the entire external os. After the acute stage subsides the chronic stage is formed. Acute endocervicitis usually is associated with acute gonorrheal exocervicitis. Chronic endocervicitis usually follows acute gonorrheal endocervicitis.

Treatment is begun within one to 5 days following the last day of menstruation. The vagina and cervix are cleaned with 2 cotton applicators.

(a) Recent, simple superficial areas of red ectropion are gently coagulated or cauterized over the entire area.

(b) Old ectropion with small cysts but without endocervicitis is treated by deep "whole erosion" cauterization or coagulation.

(c) Old ectropion with chronic endocervicitis is coned out widely, followed by vaginal packs of floroquin or negatan and cotton. The packing is done twice a week for 3 weeks. After 3 weeks the patient douches with 5 tablespoons of vinegar to her douche bag, 2 to 3 times a day for one month.

bit more over the diagnosis, but the reward is that such patients have a fine chance for cure. There are two old sayings in this connection which are still true, and will always be true; (1) The doctor who always has cancer "on the brain" is the one most likely to make early diagnoses; and (2) The easier the diagnosis of cancer the worse the prognosis.—Ed.)

## STUDIES ON THE RED FLUORESCENT PORPHYRIN DEPOSITS ON VAGINA AND CERVIX; A POSSIBLE AID IN THE DETECTION OF MALIGNANCY

E. G. JONES, H. N. SHAW AND F. H. J. FIGGE

*Am. J. Obst. & Gynec.*, 51: 467-479, 1946

The authors' interest in the relation of porphyrins to gynecologic problems stems from the postulate that there may be etiologic factors preceding, and sometimes accompanying, the development of carcinoma of the cervix. Previous work which supported this hypothesis led to the supposition that the presence of porphyrins may, on occasion, lead one to suspect a carcinomatous lesion of the cervix which otherwise would not be detected.

The authors have made a study of normally menstruating women to determine the frequency of red fluorescent (porphyrin) deposits at different phases of the menstrual cycle. Determinations were made by the inspection of vaginal tampons for fluorescence. Areas of fluorescence were described according to intensity as traces, slight, plus 1, plus 2, plus 3 and plus 4.

It was found that 10 per cent of the women studied showed large amounts of this red fluorescent material immediately following each menstrual period, about 28 per cent more showed fairly large amounts following one menstrual period, but not after every menstrual period, while 62 per cent of the women showed only traces or no porphyrin postmenstrually.

Culture from swab of the cervix of some of these women showed porphyrin producing organisms of staphylococci, streptococci, actinomyces, diphtheroids and coli. Biopsy of the cervix of a representative group of these showing red fluorescence and a control group of others not showing fluorescence failed to demonstrate any evidence of microscopic change produced by this material.

A survey of red fluorescent deposits intermenstrually revealed that traces of red fluorescent material in the vagina are not uncommon at this interval, but intensely red fluorescent secretions are rare enough to be regarded as abnormal. The latter finding may possibly prove to be a diagnostic aid in the detection of abnormal uterine flow, not associated with gross bleeding. The authors outline the limitations and possibilities of this test. The test for this red fluorescent material is simple and dramatic, and it requires no special apparatus to determine its presence other than a standard "black lamp outfit." The test is not a substitute for examination, biopsy, curettage, or any of the tests now in use for the detection of malignancy, but may be used as an adjunct to present methods, and should aid in focusing attention on the problem of carcinoma of the uterus.

Intermenstrual pain and dysmenorrhea are referred to in the symptomatology. Both are due to the increasing secretion of mucus by the cervical gland in response to the estrogens. The cervix appears large, hard and nodular, due to the presence of retention cysts on its surface. It is more or less fixed, according to the extent of infiltration of the paracervical tissues.

As to its histogenesis, the author favors both the migratory and celomic müllerian theories, and like Goodall, is inclined to believe that this condition represents a pathological endocrine activity and imperfect metabolism. Differential diagnosis ought to be made with cysts of the vagina and endometriosis.

Treatment by simple removal of the gross lesions is advised in young women presenting no other allied conditions, although recurrence is apt to occur. When endometriosis coexists and if the patient is young, a bilateral partial oophorectomy is justified. Androgenic therapy can also be of help.

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The writer reports two cases of endocervicosis, the first having been previously referred to at the Brazilian Gynecological Society in 1943.

First case: A 30 year-old patient complaining of intense secondary dysmenorrhea. Menstruation 11/2/28. Had had one child 7 years ago and 3 criminal abortions. Pelvic examination revealed in the left fornix, adjacent to the left cervical wall, a round, sensitive nodule, vesicular in appearance, and on the right side, three other smaller ones located within the vaginal wall. The cervix appeared normal. Uterus retroverted and fixed and both parametria sensitive and thickened. Reexamined at the premenstrual phase, the nodules were extraordinarily sensitive. With a previous diagnosis of vaginal endometriosis, the larger nodule was extirpated and the others electrocoagulated. Histopathologic examination revealed the presence of occasional cervical glands and mild chronic inflammatory reaction, thus leading to the diagnosis of endocervicosis.

Second case: A 54 year old patient had had her menopause 10 years ago. For the past 8 months she had complained of slight bloody vaginal discharge. Pelvic examination was negative. Endometrial biopsy revealed nothing. Cervical biopsy showed a chronic cervicitis. Due to increase of the symptomatology, a vaginal hysterectomy was performed, followed by uneventful recovery. One month later, however, patient started complaining of pain in the vagina. Pelvic examination showed a red granular lesion located in the surgical scar of the vagina. It was extirpated and the histopathological examination revealed the presence of endocervical glands lined by tall cells with light cytoplasm containing granules of mucin, and dense fibrous stroma with elastic fibers and inflammatory reaction.

(The mere fact that ectopic cervical glands are found deep in the cervical stroma or even in the paracervical tissues, or that they exhibit the "well-known cyclical changes" which I do not think are so well known in the case of the cervical glands, does not justify the designation of endocervicosis. Under the influence of chronic inflammation it is common to note marked adenomatous proliferation of the glands, and they may be found far away from the cervical canal. Moreover, they are often found beneath the squamous epithelium of the pars vaginalis as far out as the vaginal fornices. When to this we add the fact that cervical glands may at times show developmental ectopia, it would, in the present state of our

(d) Chronic endocervicitis with no ectropion is treated by wide but shallow conization followed by the after treatment described above.

(e) Large chronic hypertrophied cervix with or without ectropion or chronic endocervicitis is treated by wide shallow conization and the same after treatment.

(f) Chronic exo- and endocervicitis with or without lacerations is treated by peelization of ectropion and wide shallow conization of the cervix, followed by floroquin and cotton.

(g) Small erosions of the cervix are treated by acidulated tablets (floroquin) and vinegar douches. Gonorrheal erosions are treated in the same manner with sulfadiazine by mouth.

During the past 10 years there have been 709 carcinomas of the cervix at Jefferson Davis Hospital. During the same period, more than 5000 cervices have been coned. So far, not one case in the 5000 coned has developed carcinoma. 2 figures.

(Five-thousand conizations in 10 years is a "powerful lot" of conizations. It would seem that in such a large number of even ostensibly normal women, an occasional case of cervical carcinoma would develop. Such findings would mean nothing unless the cases have really been meticulously followed up for many years—no mean job with 5000 women. While chronic irritative lesions of the cervix are still looked upon by most gynecologists as probably playing at least some predisposing role in cancer, I have been impressed with the fact that many of our early cases, including quite a number of accidental "lucky finds", have been in cases showing little or no evidence of chronic cervicitis or erosion.—Ed.)

## "ENDOCERVICOSIS"

ALVARO DE AQUINO SALLES

Anais Brasileiros de Ginecologia, 19: 1-12, 1945

According to the writer, endocervicosis is defined as an heterotopic differentiation of the cervical glands, which, under hormonal influence, undergo cyclical changes similar to those of normally located glands. This condition has already been reported in the literature. Thus, Sammartino, in 1934, published an article on "Heterotopic proliferation of the endocervical mucosa. Cervical adenomyosis". In 1940, J. von Torzsay-Kiss reported some similar cases as "Endometriosis of cervical origin". In 1943 Goodall refers to a new disease characterized by an invasion of the deep tissues, cervical and paracervical, by the endocervical mucosa.

Pathologically, endocervicosis is characterized by the heterotopic cervical glands, with their well-known structure and functional activity in contiguity with a fibrous tissue. The glands may extend to the adjacent tissues and penetrate deeply throughout the cervical structures. According to Goodall, a diagnosis of endocervicosis can be made only when the condition has become extra-cervical and has invaded the deep paracervical tissues.

The common teachings of "biopsy every suspicious lesion" cannot be emphasized too strongly. In this instance the correct diagnosis would never have been made had this procedure not been employed. 2 figures.

(While decidual reaction in the cervix is relatively rare, we have over the years seen a good many instances in our laboratory. In some cases only small patches of decidual cells are seen, but at times broad fields of cells, as typically decidual as those seen in the endometrium, are noted. I heartily endorse what the authors say as to the importance of biopsy in all suspicious lesions of the cervix.—Ed.)

## ADENOMYOSIS

F. B. NOWLAN

J. Bowman Gray School Med., 4: 20-25, 1946

Adenomyosis has been defined by Novak as a condition characterized by a benign invasion of the endometrium into the uterine musculature with a diffuse overgrowth of the myometrium. The term adenomyosis is used loosely and is quite frequently confused with adenomyoma. It is suggested that the word adenomyosis be used as defined in this paper and no other term be used for the defined condition.

Adenomyosis is always associated with myometrial hyperplasia and the endometrial islands are not associated with collection of blood within the myometrium. Examination of the cut surface reveals a trabeculated whorl-like appearance with indefinite nonencapsulated areas consisting chiefly of concentrically hypertrophied myometrium about the endometrial islands. The myometrium is generally firm, sometimes hard. Microscopically the important feature is the abnormal presence of endometrium within the myometrium.

Many theories have been advanced as to the etiology of adenomyosis with the most widely accepted theory being that the condition represents a simple benign invasion of the myometrium by normal endometrium. The actual mechanism of such a phenomenon is not clear, but it has been suggested that normally the myometrium exerts a certain physiological pressure against the invasion by the endometrium, with which it is in direct and constant contact, and the loss, absence or diminution of such pressure may permit invasion or intermingling.

Adenomyosis is a fairly common pathological lesion, having been reported in from 1.6 to 8.6 per cent of gynecological cases. It is a progressive lesion which, in most instances, starts after 35 years of age; most frequently it is found in women between the ages of 35 and 50 years.

Fibroids of the uterus are encountered in 40 per cent of cases of adenomyosis and endometriosis in approximately 20 per cent. No investigator has been able to demonstrate an association between uterine carcinoma and previous adenomyosis.

Multiparous women are more commonly affected than primiparous or nulliparous women. Almost 50 per cent of 140 cases of adenomyosis investigated

knowledge, be rather hard to make out a good case for endocervicosis as a condition analogous to internal endometriosis or adenomyosis. I have personally seen no cases in which I felt justified in making this diagnosis.—Ed.)

## AN UNUSUAL DECIDUAL REACTION IN THE CERVIX

JOSEPH KLEIN AND L. H. DOMEIER

Am. J. Obst. & Gynec., 51: 423-426, 1946

Normally the mucous membrane of the cervix does not participate in the formation of the decidua. However, according to Novak, ectopic islands of decidual reaction may be observed in the cervix, the reaction being considered a metaplasia involving patches of mesenchymal cells which are sensitive to the hormones elaborated during pregnancy. The observation of an unusual variation of a rare pathologic entity warrants the reporting of the following case.

The patient, a 23 year old primigravida, was first seen on July 20, 1944 and the date of confinement was estimated as January 31, 1945. Examination of the cervix revealed no polyps, erosions or new growths and no unusual changes were observed on December 12, 1944. On February 6, 1945, the patient experienced a painless vaginal hemorrhage of about one cupful of blood. She was admitted to the hospital, at which time there were no evidences of shock, acute anemia or toxemia of pregnancy. The sudden onset of painless vaginal bleeding with no gross evidence of premature separation of the placenta led to a presumptive diagnosis of placenta previa. Preparations were made for possible abdominal delivery. Vaginal examination revealed no evidence of placenta previa. The external os of the effacing cervix was dilated one and a half fingers' breadth. The entire anterior lip of the cervix was replaced by an extremely soft, friable mass, the gentlest manipulation of which resulted in profuse bleeding. No polyps or erosions were visible or palpable. Since parturition appeared imminent, further investigation was postponed. Following a labor of 5 hours and 45 minutes, a living child was delivered; expulsion of the placenta and membranes was not followed by undue bleeding. A biopsy was obtained from the cervical lesion, exposing a raw surface which bled so profusely that it was necessary to insert chromic catgut ligatures to secure hemostasis. The postpartum course was uneventful. The pathologic diagnosis was decidual reaction of the cervix.

This case is unusual in that decidual reaction in the cervix was not associated with polyps. Furthermore, microscopic examination of the biopsy suggested more than the ordinary type of decidual reaction. Marked histologic variations of the decidual cells seen at and below the free margins of the specimen, as contrasted with a more mature cell-type present at the site of amputation, indicates, the authors believe, an unusual degree of cellular activity. Also, the presence of cervical glands encompassed by pleomorphic decidual cells, plus a papillary-like architecture suggests invasive potentialities. A biopsy of the cervix at 4 weeks post partum revealed no evidence of a decidual reaction or malignancy.

The case is reported of a woman, 57 years of age, in whom the menopause had occurred 3 years prior to her admission to the hospital. Seven weeks before admission she had noticed a slight spotting of blood. Examination revealed that the uterus was enlarged to about the size of a pregnancy of 4 months' duration. Total hysterectomy was performed and the specimen was sent to the pathological department.

Microscopic examination revealed the presence of a large amount of normal fat tissue, supported by a fibrous framework. While fat comprised about 70 per cent of the tumor, fibrous tissue predominated in some areas. A diagnosis of lipofibroma of the uterus was made. 1 figure.

(As mentioned by the author, lipomata of the uterus are exceedingly rare. In our laboratory we have seen a small number of myomata containing large areas of genuine fat, not only from a gross standpoint but on the basis of differential staining. The theories enumerated by the author are those commonly suggested for the histogenesis of fatty tumors in the uterus. Where real fat is found in a myoma, it would seem that the tumor is probably a mixed one, in the sense of arising from two different *anlagen*.—Ed.)

## A CASE OF INTESTINAL OBSTRUCTION ASSOCIATED WITH COMPLETE PROCIDENTIA

DOREEN DALEY AND E. N. CALLUM

J. Obst. & Gynaec. Brit. Emp., 53: 68-69, 1946

The authors present the case of a 62 year old woman who was admitted to the hospital with the complaint that "the womb had been coming down for the previous 10 months." Her bowels had not moved for 2 days and she had been unable to retain food or liquids for 5 days.

Examination revealed slight general distension of the abdomen, a reducible umbilical hernia, no visible peristalsis, shifting dullness in the flanks and increased bowel sounds. At the vulva a complete procidentia could be seen. The cervix was eroded and covered with a foul discharge. From a round opening, one inch across, in the posterior fornix, there extruded a coil of small intestine, some 18 inches long, with its mesentery. In the middle of the loop there was a gangrenous area and on the left side of the intestine there was another gangrenous organ, supposed at the time to be the appendix.

At laparotomy it was found that the last 2 or 3 feet of ileum had been dragged down into the pelvis with 18 inches of it actually prolapsed through an aperture in the everted pouch of Douglas. The ileum was resected at the level of the pelvic brim and a side-to-side anastomosis was performed between the proximal loop of the ileum and the transverse colon. The resected loop of bowel was withdrawn from the hold in the posterior fornix. The structure which had been taken for the appendix was found to be the left Fallopian tube, and this was ligated at its base and removed. In spite of transfusion and other measures, the patient died some 24 hours later and an autopsy was not obtained.

by Dreyfuss had had more pregnancies than deliveries. It is suggested that repeated childbirth or abortions play a rôle in the genesis of adenomyosis.

The most frequently encountered symptoms are metrorrhagia, menorrhagia and lower abdominal and back pain.

Since adenomyosis occurs predominately in women who have had one or more pregnancies and who are nearing the end of their reproductive period, surgical removal of the affected uterus is the usual form of therapy.

(That the origin of the aberrant endometrium in cases of uterine adenomyosis is from the surface mucosa should not be spoken of as a theory, for this explanation was demonstrated beyond any doubt many years ago, especially through the pioneer work of Cullen and Meyer. The earlier viewpoint championed by Von Recklinghausen, to the effect that the endometrial islands are of mesonephric origin, has long since been disproved. His mistake, which now seems so patent, was not unforgivable, as his work was based upon the study of hand-cut sections, which made serial study difficult and unreliable. The microtome did not come into use until some years later.—Ed.)

## LIPOMATA OF THE UTERUS, WITH REPORT OF A CASE

J. D. HICKS

M. J. Australia, 1: 184-185, 1946

A tumor of the uterus containing fat cells is of interest in that less than 50 such tumors have been recorded in the literature and some speculation is excited as to the origin of fatty tissue in this organ.

About  $\frac{1}{3}$  of the reported specimens appear to be simple lipomata and the majority contain a good deal of fibrous tissue or smooth muscle. A small percentage of the tumors are sarcomatous in nature, the malignant activity being found more in the muscle cells than in the fat. The clinical histories of these patients with fatty tumors are similar to those of patients with fibromyomata. The majority of the tumors are found in the fundus of the uterus. The presence of fat may be suspected by the pale yellow color of the tumor or by its soft consistency. The fat content of individual tumors varies from one area to another, but the larger tumors are likely to contain greater proportions of fibrous or muscular tissue.

Three possible sources of the fat cells in these tumors are:

(1) They may arise from cells which retain the potentiality of differentiating into fat cells—from the totipotent primitive mesenchymal cell—or from unipotent cells in embryonic rests of Cohnheim.

(2) There may be a metaplasia of already differentiated cells in the uterus, a transformation of connective tissue or of fibrous or muscular tissue into fat.

(3) Connective tissue cells, or muscle cells, of uterine origin may undergo fatty degeneration.

It seems reasonable to attribute the fat cells of the true lipomata and of most of the fibromyolipomata to cells laid down in the *Anlage* of the uterus, which have retained the potentiality of developing into mature adipose tissue.

(This unusual case is of much interest, showing not only that in a uterus of this completely duplicate type, apparently a uterus didelphys, a normal full term pregnancy and labor may often occur, but also that a twin pregnancy, with a fetus in each of the two uterine cavities, may progress to full term and eventuate in normal delivery. In general these duplicating anomalies call for conservative obstetrical management, although there seems to be no doubt that there is a somewhat increased incidence of miscarriage, and that in some cases dystocia may call for operative management.—Ed.)

## UTERUS DIDELPHYS

HARLEY E. ANDERSON

Am. J. Obst. & Gynec., 51: 699-701, 1946

This case report is presented to add another case of uterus didelphys to the literature. It also differs from many others in that this patient was seen late in the childbearing age, although only a few months after marriage.

A 38 year old nullipara entered the hospital complaining of severe disabling dysmenorrhea. Laparotomy had been performed 5 years previously, revealing a double retroflexed uterus and double vagina. A Baldy-Webster uterine suspension had been done.

At examination with iodized oil injected into the right cervical os, the oil failed to enter the uterine cavity. When the cannula was introduced into the left cervical opening, the iodized oil flowed freely into the endometrial cavity and left fallopian tube.

A subtotal hysterectomy was done and, upon opening the uterus, the right endometrial cavity was found to be completely obliterated by a fibroid tumor. The left side of the uterine corpus contained a very narrow endometrial cavity. 2 figures.

(Some years ago I saw a patient with uterus didelphys and with multiple myomata of moderate size in both uteri, so that a double hysterectomy was done, as she was then in her forties. This woman had in earlier years passed through two normal pregnancies, with normal labors.—Ed.)

## THE DISTRIBUTION OF THE NERVES TO THE ADULT HUMAN UTERUS

ANN FREEMAN

Am. J. Clin. Path., 16: 117-123, 1946

In this paper the author summarizes the anatomic distribution of the extrinsic and intrinsic nerves of the human uterus and adds the results of a re-examination of the distribution of the extrinsic nerves as they enter the peritoneal connective tissues laterally.

The question arises as to the cause of the perforation. There was no history of trauma to the prolapsed vaginal wall. If the perforation was spontaneous, the authors believe this case to be unique. 1 plate.

(In this unusual case the patient obviously had a large pelvic enterocele in association with her complete prolapse. While there was no history of trauma, it would be easy to understand how even slight trauma would bring about the prolapse of the intestine in this patient, or how a decubitus ulcer might bring about the same effect. In a large enterocele of this sort there is nothing between the bowel and the outside of the body except the peritoneum, a delicate areolar layer, and the overlying mucosa.—Ed.)

## "DOUBLE PREGNANCY IN A UTERUS BICORNIS" ADENOMYOSIS

FRANCISCO JAIME AND SEVERIANO G. CRISTOBAL

Anales del Ateneo del Instituto de Maternidad y Asistencia Social, Buenos Aires, 223-229, 1945

The authors report a very interesting and unusual case of double pregnancy occurring in a uterus bicornis bicollis, each of the full term fetuses lying in each half of the uterus. Both of them were alive and healthy, weighing respectively 2,300 and 2,800 grs.

The case report concerns a 35-year-old patient who had had 5 full term pregnancies and normal labors. The sixth and last one had been of twins, premature (7 months) with spontaneous delivery.

On examination, a full term pregnancy was observed. The abdomen was very much enlarged, rounded and bilobular, since the tumor was divided into two halves, both of them contracting simultaneously and presenting fetal parts. One cervix could be felt, thick and soft. A diagnosis of twin pregnancy in a probable septate uterus was then made. However, on a second examination, another cervical orifice was noted. Therefore, two different cephalic poles could be palpated through both orifices, being separated by a fleshy septum measuring 3 millimeters in thickness. Then a diagnosis of double pregnancy in a bicollis type of double uterus was established.

The patient delivered first the fetus on the left side, followed soon after by the one on the right side, labor occurring simultaneously although independently. On palpating the abdomen in order to observe uterine retraction, two distinct uteri could be felt. The convalescence was uneventful, the patient being discharged 8 days later.

A hystrogram performed months later confirmed the uterine anomaly: there was one vagina, two distinct although united cervixes and two bodies entirely independent of each other.

According to further information obtained, it seems quite probable that the patient's previous twin pregnancy was really more apt to have been a double pregnancy too, occurring in the same manner. This case represents the first one to be reported in the Argentine literature.

## THE ADNEXA

### THE CONTRIBUTION OF THE THECA INTERNA CELLS TO THE FORMATION OF THE HUMAN CORPUS LUTEUM

W. W. GREULICH

Anat. Rec., 94: 464-465, 1946

Three different views on the histogenesis of the corpus luteum have been advanced: (1) that it arises exclusively from the cells of the membrana granulosa (Sobotta, R. Meyer, R. Schroeder, et al.); (2) that the granulosa cells degenerate and that the luteal cells are derived exclusively from the cells of the theca interna (C. H. von Baer, His, Koelliker, et al.); and (3) that both the granulosa and the theca interna cells contribute to its formation (Waldeyer, Luschka, et al.).

In the present study, corpora lutea of various ages were obtained at operation from young women in whose reproductive organs there was no gross evidence of disease. The specimens were fixed immediately in Bouin's acetic mixture and one-half of each was embedded in paraffin and the other half in celloidin. Sections were cut at 5 or 6 micra.

Kodachrome photomicrographs of these sections demonstrated that, contrary to what is now the generally accepted view, the theca interna cells appear to contribute significantly to the formation of the human corpus luteum. A study of similar preparations from a young, human corpus luteum of pregnancy suggests that the theca interna cells continue to be added to it throughout its functional life.

(I believe that some injustice is done to men like Meyer and Schroeder in attributing to them the belief that the corpus luteum arises exclusively from the cells of the membrana granulosa. They undoubtedly hold the view, as does everyone else, that the lutein cells of the corpus luteum are of granulosa origin, but they certainly do not overlook the fact that the theca interna contributes to the formation of the corpus luteum. This is apparent even on the simplest histological examination of any mature corpus luteum. Well marked septa of the theca interna divide the lutein cells into compartments, and these theca cells themselves often show luteinization changes, though always readily distinguishable from the granulosa lutein cells. The name of paralutein cells was given to these theca lutein cells by an Italian investigator, Pinto.—Ed.)

### "FOLLICULAR CYST SIMULATING A CORPUS LUTEUM CYST"

WASHINGTON BRUNO

Archivos de la Sociedad Argentina de Anatomia Normal y Patologica, 6: 232-241,  
1944

The writer reports an unusual and interesting finding on an ovary removed from a 42 year-old patient with retroversion and myoma of the uterus, four days prior to menstruation.

According to the literature, nonmyelinated and myelinated extrinsic nerves extend from the abdominal segments of the spinal cord to form the mesenteric and hypogastric plexuses. Trunks coursing from these plexuses enter Frankenhauser's ganglia making synapses here, and extend medially to enter the uterus at the uterocervical junction. According to many accounts, these trunks in the peritoneal connective tissues of the uterus divide outside the myometrium into branches which extend upward toward the fundus and downward into the cervix to form the intrinsic nerve supply of the uterus.

These relations were re-examined in serial sections from a nulliparous uterus, obtained immediately postmortem from the body of a 14 year old girl. Grossly the uterus showed no unusual changes.

Microscopic examination of these sections showed that large nerve trunks approach the uterus laterally on both sides of the cervix in the loose connective tissue. These trunks are accompanied by large branches of the uterine arteries into the myometrium. Small and medium-sized ganglion cells were found in the large trunks in the extrauterine tissues at a level corresponding to the internal os. Structures identified as Vater-Pacinian corpuscles were connected with large trunks and branches of the nerves as they entered the connective tissues slightly above the uterocervical junction. At this level, branches from the large trunks accompanied blood vessels, entering the cervical wall parallel to the cavum and extended inward. Outside the myometrium these trunks divided into branches which extended upward toward the fundus and downward through the cervix. These branches extended into the inner half of the myometrium. Other large nerve trunks, less numerous, passed along the lateral sides of the uterus and also accompanied large blood vessels. At a level corresponding to the fundus large branches ascended in the connective tissue of the broad ligament, entering the myometrium parallel to the cavum and divided immediately. Several nerve trunks sent fibers into the inner fourth of the myometrium and into the basal layer of the endometrium. The number of trunks diminished from the level of the internal os toward the fundus. 2 figures.

These structures, which have never been described before, consisted of small, free annular formations found in the ovarian stroma, mainly at the periphery of the corpus albicans and usually within the clear space lying between the latter and the reticular framework, or in the connective centre of the corpus luteum; thus, in places where the reticulum exhibits transformation or growing phenomena. They show the staining reactions of the reticulum and at times they are attached to the fibers of the latter by means of a sort of pedicle. The annular filament is usually homogeneous and the lumina empty, with no fat reaction such as is seen in the lutein cells.

Since they are found in those areas where active growing or transformation of fibers is observed, the author is inclined to believe that these structures are related to the formation of reticulum fibrils, which should be possible according to the "inobionas'" theory of Cajal-Rio Hortega, by which the connective fibers are made up of functional units called "inobionas", just as the nerve fibers are made up of "neurobionas".

By means of local factors, these elements could possibly be liberated from the fibrils where they are formed, and by division or conglomeration arrange themselves in a linear way, thus giving rise to a reticular or collagenous fiber.

## "ETIOLOGY OF ENDOMETRIOSIS"

CONRADO ZUCKERMANN

Ginecologia y Obstetricia de Mexico, 1: 47-52, 1946

In a brief review the writer summarizes the different etiologic factors and histogenetic theories brought forth to explain the occurrence of endometriosis.

According to the writer, this disease is better explained on an endocrine basis. Thereby, estrogens in larger quantities or persisting for an exceedingly long period of time, cause overgrowth of the endometrium. The endometrial cells may then migrate through intercellular spaces, lymphatics or veins into the uterine wall and pelvic cavity, where they can lodge and grow.

The same estrogenic factor produces at the same time ovarian, peritoneal, tubal, uterine and perhaps vaginal sclerosis too, and may contribute to the development of myomas and fibromas.

The excess of estrogens may be related to a deficiency in the production of progesterone. Therefore, by normalising the level of one of these hormones, it is possible to obtain a normal balance of the other.

Progesterone facilitates the excretion of estrogen and thereby its diminution in the pelvic area.

(The author's easy solution of this vexed question is of course based on no available evidence. Few will deny that hyperplasia of the endometrium is due to such excessive or persistent estrogen stimulation, but it is a far cry from such hyperplasia to the endometrial

Grossly it looked very much like a cystic corpus luteum the size of a hazel-nut, containing clear fluid within its cavity, which seemed to be epithelialized. However, careful microscopic examination showed it to be a solid corpus luteum surrounding almost entirely an adjacent follicle cyst, thus very closely resembling a lutein cyst.

Histologically the wall of the cyst presented four distinct layers of cells: 1) an external one of connective tissue cells, in connection with the ovarian stroma; 2) typical lutein tissue with paralutein cells on its external surface; 3) a layer of fibrous tissue with hemorrhages and blood vessels, representing the former centre coagule of the corpus luteum, surrounded internally by another layer of lutein tissue and paralutein cells; 4) a vascular connective tissue. Close to the lumina there were several cells forming a discontinuous epithelial lining, thus looking exactly the same as the lumina of a follicle cyst, which is lined by an epithelial layer that can be later on partially or totally cast off.

It is quite possible that such a picture may be reproduced when two follicles are growing close to each other. As one of them ruptures to become a corpus luteum, the neighbour one undergoing cystic changes continues to grow and presses against the collapsed one, causing its invagination. Hence, the corpus luteum on developing encircles the latter almost entirely.

The writer is inclined to believe that such a disposition may constitute what has been improperly designated as groups III and IV of lutein cysts (lumina presenting flat or columnar epithelial lining) according to Fraenkel's classification (1898), the interpretation of which has aroused much discussion, although no satisfactory explanation has been offered.

(This is an interesting histological observation, and the author's explanation of the rather confusing picture of a corpus luteum apparently engulfing an adjacent follicle seems to me to be a valid and plausible one. Anyone accustomed to examining ovaries microscopically must have noted how a growing corpus luteum not infrequently adapts its direction of growth to adjacent structures, and also vice versa. It is quite possible also that the picture of a low epithelial lining of the lumina of corpora lutea reported by some of the older authors may have been produced by just such a process as the author has described.—Ed.)

## "CONCERNING A PECULIAR DISPOSITION OF THE OVARIAN RETICULUM AND ITS POSSIBLE SIGNIFICANCE"

WASHINGTON BRUNO

Archivos de Histologia Normal y Patologica, 2: 531-540, 1945

By using the Rio Hortega's method of impregnation (double impregnation with silver nitrate and carbonate) following previous treatment with potassium permanganate and oxalic acid, the author was able to demonstrate some very peculiar structures on examining sections of human ovary.

lower abdominal pain or intractable dysmenorrhea without relief. Endometrial lesions of varying extent were overlooked or misinterpreted. The authors emphasize the fact that endometriosis should be given its proper place in the diagnostic armament of general surgeons, internists, endocrinologists, urologists and physicians in general practice.

The authors have divided their cases of intestinal endometriosis into 2 main groups: (1) those having endometriosis involving the rectum, and (2) those having the lesion higher up in the intestinal tract. In 41 cases in which the rectum was involved, the 4 commonest symptoms, in order of frequency, were lower abdominal pain, rectal pain or pain with bowel movement, dyspareunia and backache. In 12 cases with endometriosis proximal to the rectum, the 5 commonest symptoms were lower abdominal pain, nausea and vomiting, rectal pain, constipation and gas and generalized distress. In both groups, the symptoms were more pronounced during menstrual time.

Endometriosis is a progressive, adhesive penetrating lesion which may require such radical treatment as castration. However, in a young woman desiring pregnancy, a supreme effort should be made to conserve ovarian function, even though only partial removal of the endometrial tissue is possible. Subsequent x-ray castration may then be resorted to if symptoms should persist or recur. Widespread lesions involving only superficial or relatively unimportant structures are surgically removed or destroyed with the nasal loop cautery. Deep lesions, such as chocolate cysts and adenomyomas, are resected in almost direct proportion to the patient's age and parity. Cauterization of the surface of deep lesions, when complete removal seems to be hazardous, frequently gives symptomatic relief.

The vaginal approach, both in diagnosis and treatment, has found increasing favor with the authors. The diagnostic use of colpotomy is of value. In treatment, the vaginal operation ordinarily should not be chosen under the following conditions: (1) In patients whose clinical symptoms suggest bowel involvement; (2) For those patients in whom sterility is of first importance; (3) Grossly extensive lesions associated with fixation of organs; (4) In instances of fixed retroversion which cannot be easily reposed; and (5) Where extraneous symptom may indicate abdominal exploration.

(A good many of the 11 symptoms enumerated by the authors are not of much value in the differential diagnosis of endometriosis, but some are, such as rectal dysmenorrhea (not necessarily merely rectal pain at defecation), dyspareunia, and sterility of unexplained origin, though there are many unexplained cases other than those with endometriosis. Perhaps more important than the symptoms are the signs on the pelvic examination in many cases of endometriosis, particularly the presence of one or more nodules in the uterosacral ligaments. These may be small, like buckshot, but in other cases as large as a cherry or much larger. They indicate uterosacral "implantation", and when present, make the diagnosis reasonably certain, especially when associated with a tender, adherent enlarged ovary or even a mass of considerable size giving the impression of a small thick-walled adherent cyst. The uterosacral involvement explains the premenstrual or menstrual pain in the rectum, lower sacral or coccygeal region.

The authors' comments on the importance of conservative surgery in the younger group of patients can be heartily endorsed. Subsequent pregnancies are not rare, and many pa-

invasion of the muscle in adenomyosis and, even more, to the ectopic occurrence of endometrium at various sites in the pelvis. The latter seems to presuppose that some vestigial sensitivity to the ovarian hormones persists at these various sites, unless one chooses to explain them all on the tubal regurgitation concept of Sampson. I have always felt that some common thread of relationship runs between hyperplasia, adenomyosis and pelvic endometriosis, and this thread may well be of endocrine nature. But this is very different from saying that all these conditions are produced by endocrine factors alone.—Ed.)

## A COMPARATIVE ANALYSIS OF THE DIAGNOSIS AND TREATMENT OF ENDOMETRIOSIS, INCLUDING A REPORT OF FIFTY-THREE CASES OF INTESTINAL ENDOMETRIOSIS

S. T. THIERSTEIN AND E. ALLEN

*Am. J. Obst. & Gynec.*, 51: 635-642, 1946

In a comparative study of the case records of 569 patients operated upon for endometriosis (previously reported) with a more recent group of 317 patients operated upon by the same surgeons during the last 4 years, certain general changes in diagnosis and treatment were noted.

In diagnosis, a carefully taken clinical history may reveal such symptoms as the following:

1. Dyspareunia.
2. Rectal pain caused by passage of stool or gas; this pain is usually present only at menstrual time.
3. Recurrent diarrhea coincident with the menstrual period.
4. Symptoms of low grade bowel obstruction at period time.
5. Unexplained sterility.
6. Extension of menstrual backache to the thigh and often to the lower leg.
7. Abnormally increased bladder irritability at menstrual time.
8. Low deep pelvic discomfort caused by jarring of the body.
9. History of acquired dysmenorrhea in a multipara or a change in type of pain of functional dysmenorrhea in a nullipara.
10. Appearance of the symptom-complex resembling that of pelvic infection in a patient over 35 years of age, since pelvic infection becomes increasingly rarer during this decade.
11. Finding of blood in the stool at menstrual time which cannot be accounted for by the commoner forms of rectal pathology.

The routine employment of combined rectovaginal pelvic examination has undoubtedly been greatly responsible for more accurate diagnosis. This should be performed on the unanesthetized patient, since exquisite "point tenderness" may direct the examiner's attention to minute nodules. Examination should be made during the menstrual period or on the day preceding the onset of menstruation.

A large number of patients in this series had been operated upon elsewhere for

of the tumor in all directions, well delimited neoplasm of medium size, tumor presenting smooth surface and solid portions); 3) x-ray plate alone or followed by hysterosalpingography may lead to a correct diagnosis whenever the tumor contains rudiments of teeth or fragments of bone; 4) in order to establish a diagnosis of dermoid cyst of the ovary, one must bear this latter possibility in mind.

(The incidence of dermoids in the rather small group of 68 ovarian neoplasms studied was 11.4 per cent, which is slightly higher than the usual figure of 10 per cent given by many authors. As a matter of fact, the latter figure is probably higher than the true incidence. A recent study of a much larger group of 225 cases by Blackwell, Dockerty, Masson and Mussey (Am. J. Obst. & Gynec., 51: 151 (February), 1946), gave an incidence of only 5 per cent, and this would seem to me more nearly correct.

The 4 conclusions drawn by Urrutia epitomize very nicely, it seems to me, the clinical considerations which should lead one to suspect that a palpable ovarian tumor is probably a dermoid cyst.—Ed.)

## OVARIAN DERMOID CYSTS

E. ROHAN WILLIAMS

Brit. J. Radiol., 19: 88, 1946

The author discusses the diagnosis of an ovarian dermoid cyst by x-ray examination. The presence of an ovarian dermoid cyst may be suspected or confidently diagnosed by the recognition of one or more of the following appearances:

(1) *Tooth formation* may be associated with limited ossification. Individual dental structures may be seen as unformed denticles or as fully developed teeth. It is more common to see groups of dental structures than a single tooth. It may be stressed that the size of the group of dental structures is no measure of the size of the cyst.

(2) *Calcification* in the wall of a cyst may be partial or complete.

(3) *Transradiancy of the cyst-mass* owing to the high fat content of the sebaceous material. An oval or rounded area of transradiancy may be seen in the pelvis demarcated by a more opaque peripheral ring. Sometimes a mottling is observed, due to the hair content of the cyst. 4 figures.

(The x-ray appearances indicated in the abstract by (1) and (2) are those commonly considered to point to the probability of a dermoid cyst, especially if a tumor can be palpated. That indicated under (3) is probably less frequently recognized. A clinical feature of dermoid cysts to which some of us attach significance is the fact that they are not infrequently palpable in front of the uterus or broad ligament, while most ovarian cysts tend to swing downward and backward. There are, however, many exceptions to this from both a positive and negative standpoint, although a Staff man can at times impress the interne by taking a chance and predicting that a cyst located as above mentioned will be a dermoid.—Ed.)

tients are relieved of their symptoms, even though there may be a residuum of endometriosis in the pelvis. Some, however, may need secondary operation later.

As to the vaginal approach, I do not believe that this will appeal to most gynecologists, and for myself, I would say that this is especially the type of lesion in which I would prefer the abdominal route. The frequent thickening and infiltration of the uterosacral ligaments and the frequent welding of the rectum to the posterior surface of the cervix and lower corpus would seem almost a priori to make the vaginal route more difficult and more hazardous. Nor does it give one the opportunity of observing the distribution of the aberrant endometrium in the pelvis and thus reaching an intelligent conclusion as to the nature and scope of the operation indicated in the particular case. Certainly it would be impossible by the vaginal route to eliminate the possibility of the intestinal involvement which the authors especially emphasize in their paper. The authors themselves call attention to these contraindications, but my impression would be that most of the cases in which they are absent would probably be those in which a reasonably positive diagnosis of endometriosis cannot be made preoperatively.—Ed.)

### "ENDOMETRIOSIS"

JOAQUIN CORREA

Ginecologia y Obstetricia de Mexico, 1: 41-46, 1946

In a brief review, the writer regards the definition, history, sites, incidence and nosology of endometriosis.

As to its frequency in Mexico, only a very few cases have been reported. This low incidence of the disease is certainly due to the lack of systematic pathologic examination of the surgical specimens that have been removed.

### "A CLINICAL STUDY OF DERMOID CYSTS OF THE OVARY"

MANUEL URRUTIA

Ginecologia y Obstetricia de Mexico, 1: 25-34, 1946

From 1938 to 1945 there were 3111 cases admitted to the Gynecological Department of the "Hospital General" of Mexico. These cases included 68 neoplasms of the ovary (2.18%), from which 7 (0.2%) were dermoid cysts. Therefore, the incidence of dermoid cysts in relation to all neoplasms of the ovary was 11.47%.

Following a brief study of these cases from a purely clinical standpoint, the author draws the following conclusions: 1) the clinical history alone does not suffice to make a diagnosis of dermoid cyst; 2) pelvic examination yields valuable information in a great number of cases, so as to permit one to suspect the presence of the neoplasm (anteposition of the cyst in relation to the uterus, great mobility

In 9 of the 21 cases in this series there was a history of amenorrhea followed by remenstruation, representing an incidence of 42.8 per cent. Five patients were classed as having premenopausal amenorrhea, or an incidence of 23.8 per cent and 4 cases were classed as postmenopausal bleeding, or an incidence of 19.05 per cent. Five cases are summarized in this paper because of the finding of granulosa-cell tumor associated with a history of premature menopause (amenorrhea with resumption of menstruation). The ages of these 5 patients were as follows: 43, 45, 40, 23 and 40 years of age. One of these patients menstruated twice after removal of the granulosa-cell tumor, and is now approximately 3 months pregnant.

The phenomena of amenorrhea followed by menstrual return is known to be the result of hormonal disturbance, but the exact mechanics of the amenorrhea in women who are far from their menopause, with a subsequent menstrual flow calls for further enlightenment. Kluft states that the prolonged amenorrhea is due to structures similar to corpus luteum or albicans in the tumor.

All patients in this series were operated upon. The diagnosis was made after operation on gross and by histologic means. Some cases were diagnosed only after microscopic examination. Follow-up studies show that all patients are living and have no evidence of recurrence.

(Without having bothered to count the cases in the literature, I feel sure that many more than 240 could be gathered. I myself have examined slides or tissue from considerably more than half that number. The bulk of these have not, of course, been from our own department, the material having been sent in from outside sources for diagnosis. In the few years of operation of the Ovarian Tumor Registry, about 25 cases of granulosa-cell carcinoma have been received. The tumor is, of course, a relatively rare one, but not nearly as rare as some appear to believe, and considerably more common than arrhenoblastoma or dysgerminoma.

Amenorrhea is not rare, in spite of the estrogen production of the tumor, just as hyperplasia of the endometrium, also an estrogen-induced lesion, may be associated with amenorrhea (polyhormonal amenorrhea). The endometrium in granulosa tumor cases is not always hyperplastic, not infrequently showing more moderate proliferative pictures corresponding to an early interval phase. Only 2 of the 21 cases reported are said to have been diagnosed as malignant, and all patients are now reported as living and well. I do not believe this gives an accurate index of the malignant potentialities of this tumor type. While certainly far less than those of the common types of ovarian carcinoma, many instances of recurrence and death have been reported. Moreover, the recurrences are sometimes late, as long as 12, 13 or even 18 years after the original operation. It will probably be a good many years before a sufficient number of follow-up studies are available to form a more accurate opinion as to the degree of clinical malignancy of this group of tumors.—Ed.)

ARGENTAFFIN CARCINOMA (CARCINOID TUMOR) ARISING  
IN AN OVARIAN DERMOID CYST

W. J. BLACKWELL AND M. B. DOCKERTY

Am. J. Obst. &amp; Gynec., 51: 575-577, 1946

While studying a large series of dermoid cysts the authors encountered a very small nodule of argentaffin carcinoma (carcinoid tumor) in an ovarian cyst.

At operation on a 59 year old woman, bilateral ovarian dermoid cysts were found and the uterus contained multiple small fibromyomas. Hysterectomy and bilateral salpingo oophorectomy were performed.

Each of the ovarian "dermoids" was approximately 8 cm. in diameter, unilocular and almost completely cystic. The content of sebaceous material, hair, and so forth, and the small "dermoid processes" were not remarkable grossly. In one of the tissue blocks routinely selected from the left ovarian tumor a microscopic-sized portion disclosed, with hematoxylin and eosin preparations, an appearance which at once suggested the diagnosis of carcinoid tumor. The cells were small, prismatic in shape, dark-staining and granular, and were arranged in islands and strands which showed a degree of palisading of the peripheral layers. Preparations on other blocks, using silver impregnation methods showed numerous argentaffin granulations in the cytoplasm. Attempts to establish the identity of the gastrointestinal tissue of origin were unsuccessful. The authors submit this case as representing the fourth example of argentaffin carcinoma (carcinoid) occurring within a dermoid cyst. 3 figures.

GRANULOSA-CELL TUMOR OF THE OVARY; REPORT OF FIVE  
CASES WITH PREMATURE MENOPAUSE (AMENORRHEA)  
AND THE RECURRENCE OF MENSTRUATION

E. E. RHOADS

Am. J. Obst. &amp; Gynec., 51: 560-564, 1946

A review of the literature shows that, to date, some 240 cases of granulosa-cell tumors have been reported. Only 21 cases were found in the records of the University Hospitals of Cleveland and of these, only 2 were diagnosed as malignant. All of these cases in which the uterus was removed or a curettage was done showed hypertrophy of the uterine musculature and hyperplasia of the endometrium.

Granulosa-cell tumors were catalogued according to the following age groups: (1) prepubescent or childhood; (2) adult (those within the range of normal menstruation); and (3) postmenopausal. All 21 cases in this series were in the second and third groups. The youngest patient was 23 and the oldest 69 years of age.

In 9 of the 21 cases in this series there was a history of amenorrhea followed by remenstruation, representing an incidence of 42.8 per cent. Five patients were classed as having premenopausal amenorrhea, or an incidence of 23.8 per cent and 4 cases were classed as postmenopausal bleeding, or an incidence of 19.05 per cent. Five cases are summarized in this paper because of the finding of granulosa-cell tumor associated with a history of premature menopause (amenorrhea with resumption of menstruation). The ages of these 5 patients were as follows: 43, 45, 40, 23 and 40 years of age. One of these patients menstruated twice after removal of the granulosa-cell tumor, and is now approximately 3 months pregnant.

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(Without having bothered to count the cases in the literature, I feel sure that many more than 240 could be gathered. I myself have examined slides or tissue from considerably more than half that number. The bulk of these have not, of course, been from our own department, the material having been sent in from outside sources for diagnosis. In the few years of operation of the Ovarian Tumor Registry, about 25 cases of granulosa-cell carcinoma have been received. The tumor is, of course, a relatively rare one, but not nearly as rare as some appear to believe, and considerably more common than arrhenoblastoma or dysgerminoma. -

Amenorrhea is not rare, in spite of the estrogen production of the tumor, just as hyperplasia of the endometrium, also an estrogen-induced lesion, may be associated with amenorrhea (polyhormonal amenorrhea). The endometrium in granulosa tumor cases is not always hyperplastic, not infrequently showing more moderate proliferative pictures corresponding to an early interval phase. Only 2 of the 21 cases reported are said to have been diagnosed as malignant, and all patients are now reported as living and well. I do not believe this gives an accurate index of the malignant potentialities of this tumor type. While certainly far less than those of the common types of ovarian carcinoma, many instances of recurrence and death have been reported. Moreover, the recurrences are sometimes late, as long as 12, 13 or even 18 years after the original operation. It will probably be a good many years before a sufficient number of follow-up studies are available to form a more accurate opinion as to the degree of clinical malignancy of this group of tumors.—Ed.)

## A CONTRIBUTION TO THE PROBLEM OF MASCULINIZATION

H. F. BETTINGER AND H. JACOBS

M. J. Australia, 1: 10-13, 1946

Masculinization of a normally developed woman is known to occur either (1) as part of a general disturbance of endocrine function or (2) as a result of a neoplasm. In the latter group the most straightforward cases are caused by arrhenoblastoma of the ovary. The development of the masculinization syndrome and its disappearance after removal of the tumor are well understood.

Greater difficulties are encountered in cases in which the disturbances are apparently produced by cells of the type of the adrenal cortex. In some of these cases a well-defined tumor of the adrenal cortex can be demonstrated but such a tumor may be absent and the syndrome ascribed to a hyperfunction or dysfunction of the adrenal cortex. Adrenal cortical cells may, furthermore, give rise to ovarian neoplasms. The authors present a case which is pertinent to the many aspects of the problem of masculinization.

The patient was a young girl, aged 14 years, who reported a noticeable swelling of her abdomen about 6 weeks prior to examination. The swelling had been associated with neither pain nor vomiting. The menarche had occurred at 12 years of age and the menstrual periods had been normal. During the last 4 weeks the patient had had several copious but painless vaginal hemorrhages.

Examination revealed some features of masculinization, including growth of hair on the face, poorly developed breasts and a hypertrophic clitoris. The abdomen was filled by a large semisolid mass.

At operation, large amounts of yellowish fluid escaped from the initial incision. A large multilocular cystic tumor was found in the position of the left ovary, attached to the Fallopian tube. The tumor, which was partly degenerated, was removed with the left Fallopian tube. The patient's recovery was uneventful and she was discharged 3½ weeks after operation. Six years later there was no evidence of a recurrence of any symptoms or signs and the masculinizing features had disappeared.

Microscopic examination of the tumor established it as a malignant pseudomucinous cystadenoma. The only unusual finding was a peculiar variation in the structure of the stroma of the tumor. Often the connective tissue was of the usual mature type. However, in some places there were found substantial amounts of a cellular tissue which was indistinguishable from luteinized *theca interna*.

The authors conclude that masculinization was produced by hormones secreted by a luteinized *theca interna* and that these hormonal disturbances were initiated by the neoplasm of the pseudomucinous group of ovarian tumors. 8 figures.

(Without having available sections or photomicrographs of the tumor described by the authors, no intelligent comment can be made as to its possible nature. A few cases have been reported, by Geist and others, in which lutein-like cells scattered throughout the

ovarian stroma appear to have caused masculinization. Certainly the pseudomucinous cystadenocarcinoma in itself could scarcely have been responsible. The whole question of sex differentiation is still far from clear, and this statement certainly applies to the apparently interlocking roles played by the adrenal and the gonads in some of these cases, as in the well known cortico-gonadal syndrome associated with certain adrenal tumors. For that matter the adrenal cannot be excluded from consideration as a possible factor in the masculinization syndrome seen with arrhenoblastoma, perhaps on the basis of the intimate embryological relation between the adrenal cortex and the ovarian medulla. I have never felt that Meyer's explanation of the masculinizing effects of arrhenoblastoma, simply on the basis of the derivation of the latter from originally male-directed cells, is the whole answer to the question.

Even more confusion exists as to the masculinization symptoms which have been reported with certain cases of luteoma. What we know as to the general nature and hormone function of lutein cells makes it difficult to believe that genuine lutein cells could exert a masculinizing effect, and it has seemed more probable that the tissue concerned in these cases is really of adrenal origin. This uncertainty has led to the convenient but defeatist application of the designation masculinovoblastoma to tumors of this doubtful character. —Ed.)

## OVARIAN INVOLVEMENT IN HODGKIN'S DISEASE

E. L. HELLER AND W. PALIN

Arch. Path., 41: 282-289, 1946

It is apparent, from a perusal of the literature, that ovarian involvement in Hodgkin's disease is infrequent. Gemmell theorized that ovarian hypofunction might be responsible for the occurrence of the disease in women, but in his series of 57 cases of Hodgkin's disease in the female he described no lesions of the ovary to substantiate this concept, which in several cases was based on a history of reduced or suppressed menstruation. That infiltration of the ovary in Hodgkin's disease can be of considerable extent is illustrated in the following 2 case report summaries.

*Case I* The patient, a 69 year old white woman, was admitted to the hospital complaining of abdominal pain, loss of 30 pounds in the previous 6 months and a cough of 3 weeks' duration.

Examination revealed a poorly nourished patient with evidence of vitamin deficiency. None of the superficial lymph nodes was enlarged and the chest was essentially normal. The abdomen was distended with evidence of free fluid and an indefinite mass was noted in the epigastrium. During the first 6 days her temperature varied, reaching 102 and 103 degrees F. Laboratory studies yielded essentially normal findings except for a moderate anemia. Signs of pulmonary consolidation developed, and although the temperature returned to normal after one week of sulfamerazine therapy, she was unable to take food, became progressively weaker and died 20 days after admission.

Autopsy revealed moderately intense pulmonary congestion and edema and

small, patchy bronchopneumonic areas in both lungs. There was 400 cc. of clear ascitic fluid in the peritoneal cavity. Throughout the omentum and mesentery were numerous prominent lymph nodes, varying from 2 to 5 cm. in diameter, their cut surfaces studded with small irregular areas of necrosis. A large, irregular retroperitoneal mass extended from the inferior surface of the diaphragm to the aortic bifurcation. This mass was composed of lymph nodes whose cut surfaces were similar to those of the mesenteric group. With the exception of the left ovary the abdominal viscera were not noteworthy. The uterus, both fallopian tubes and the right ovary showed advanced involutionary atrophy; the left ovary was irregularly enlarged. It was in normal position, was freely movable and no enlarged lymph nodes were in close proximity. The capsule was intact. On section an irregular nodular mass was seen replacing the bulk of the stroma. The cut surface of the tissue was similar to that of the abdominal lymph nodes.

Microscopic examination revealed 2 types of lesions. Throughout the abdominal lymph nodes, which were regarded as the primary site, the picture was that of Hodgkin's sarcoma (Karsner) with large irregular reticuloendothelial cells spreading diffusely throughout the interstitial pulp and sinusoidal spaces, and exhibiting numerous mitotic figures. Pleomorphism was particularly pronounced. The second type was that designated as Hodgkin's paraganuloma (Jackson and Parker), in which the infiltrate consisted of masses of closely spaced lymphocytic cells of mature type, containing few of the larger reticuloendothelial cells which characterize Hodgkin's disease. Both of these types formed the ovarian tumor. Although the characteristic granulomatous reaction was not observed in this case, if one accepts the broader concept of Hodgkin's disease as one with a variable pattern, subject to mutations and transitions in which the tumor changes into the sarcomatous and almost pure lymphoid variants, the diagnosis becomes tenable.

*Case II.* A 35 year old white woman was first seen with the complaint of continuous pressure and cramplike pains in the right lower abdominal quadrant and progressive abdominal enlargement of 6 weeks' duration. Abdominal examination revealed a firm non-tender mass in the epigastrium. Pelvic examination revealed an irregular, firm nodular mass in the region of the right ovary. Similar nodules were felt in the cul-de-sac. Laboratory studies were noncontributory and the clinical impression was that of ovarian cancer with metastatic involvement of the abdominal lymph nodes.

At laparotomy the right ovary and a biopsy specimen of the omentum were removed. A large solid mesenteric mass, firm and fixed on all sides, was noted in the epigastrium. Recovery was uneventful and the patient was discharged on the 16th postoperative day.

Pathological examination revealed a greatly enlarged ovary covered by a thin intact capsule. On section the parenchymatous and stromal elements were found to have been largely replaced by a heavy cellular infiltration associated with considerable fibrosis. The predominating cells were of lymphoid type, the majority being typical mature lymphocytes tightly packed in large numbers.

The occurrence of larger cells of reticuloendothelial type, resembling poorly developed Sternberg-Reed cells, scattered eosinophils and the fibrosis led to a diagnosis of lymphoblastoma, probably Hodgkin's disease. A similar infiltration was noted in the omentum.

Following this report a discrete subcutaneous nodule was detected in the patient's right arm. When this was excised and examined, sections revealed a lymph node showing a diffuse lymphoid infiltration of the germinal centers and interstitial structure and reticuloendothelial cells; in the peripheral areas larger reticuloendothelial cells of the Sternberg-Reed type were numerous.

That the ovarian involvement in both of these cases was not the result of fusion with, and direct extension from, contiguous lymph nodes was manifested by the fact that the organs were freely movable, in normal position, unattached to neighboring nodes and each surrounded by an intact ovarian capsule. In Case I sarcomatous cells were identified within the lumen of veins within the substance of the ovary. This probably serves to explain the genesis of the infiltration in this organ. 2 figures.

(I have personally observed no instance of this type, although I have seen 2 cases of lymphosarcoma of the ovary, both apparently secondary to lymphosarcoma elsewhere in the abdominal cavity. The photomicrographs accompanying the authors' paper seem to justify their diagnosis. Since one is apt to think of Hodgkin's disease as a disease characteristically involving lymph glands, it is difficult to explain the involvement of such an organ as the ovary.—Ed.)

## FEMALE UROLOGY

### AN EVALUATION OF METHODS FOR THE TREATMENT OF URINARY INCONTINENCE

ALBERT H. ALDRIDGE

Am. J. Obst. & Gynec., 51: 299-315, 1946

Out of the variety of conditions, well known to cause urinary incontinence, 2 major causes are responsible in a high percentage of patients. They are obstetrical trauma and damage to tissues from malignant neoplasms either alone or in combination with irradiation therapy used to eradicate such growths. Incontinence of urine resulting from these injuries may be due to fistulous communications between the urethra, bladder or ureters and the vagina or uterus. However, the most frequent cause for loss of urinary control is incompetence of the urethral sphincter mechanism which controls urination.

The literature reveals that van Roonhuysen, 1663, was the first to "discover and put into execution a well-defined plan of operative treatment." His technique, as recorded, is interesting. With the patient in the lithotomy position, the fistula was exposed with a speculum. The margins of the fistula were denuded and brought into apposition with sharpened goose quills which were held in position by silk threads. The wound was dressed with flat wicks moistened with warm balsam oil and the vagina was filled with sponges saturated with the oil of sweet almonds. Jobert deLamballe was probably the first to emphasize the importance of avoiding tension on the margins of a wound. Contributions of other surgeons include: (1) "flap splitting"; (2) free mobilization of the bladder and separate suturing of the bladder and vaginal walls; (3) suprapubic extraperitoneal closure of vesicovaginal fistulas; and (4) suprapubic transperitoneal operations for urinary fistulas.

Sims' contributions to the original procedure for closure of a fistula (denudation of its margins and closure with some form of interrupted suture material) included improved exposure of the fistula and the use of silver wire sutures and certain instruments developed to insure exact placement and adjustment of these sutures. The author's experience with the Sims technique has brought the conviction that it is best suited for the closure of small to moderate-sized urethral and bladder fistulas which are reasonably accessible and are located on relatively flat surfaces.

At present, operative techniques for closure of urinary fistulas are based on the original techniques. The modern preparation of the patient for operation includes not only steps to eliminate urinary infection but also measures to improve the general health of the patient. Successful operation depends upon accurate localization of the fistula and selection of a technique best suited to conditions found before and at the time of operation. Repair of a fistula by a

technique which depends upon denudation of its margins should never be attempted unless closure can be accomplished without undue tension on the surrounding tissues. Flaps developed for closure of a fistula should be made up of the entire thickness of the vaginal wall to insure optimum nerve and blood supply. The importance of closing a fistula with the first attempt is obvious. Every surgical failure decreases the chance for ultimate success.

Vaginal plastic procedures are successful in curing about 80 to 90 per cent of patients who have urinary incontinence due to relaxation or partial destruction of the urethral sphincter muscles. If function of these muscles cannot be restored by vaginal plastic procedures, an attempt to establish urinary control by transplantation of adjacent muscles and fascia should be considered. A tech-

TABLE II  
*Summary of treatment of 118 urinary fistulas*

TYPE OF FISTULA	NO.	OPERATION							RESULT OF TREATMENT					
		None	Sims	Flap	Implant of ureters to		Nephrectomy	Other	Palliative		Operative			
					Bladder	Bowel			Unchanged	Spont. healing	Cured	Improved	Fatal	Died
Vesicovaginal.....	75	18	23	32		1		1*	15	3	48		7	2
Urethrovaginal.....	14	4		9				1†	4		8	1		1
Urethrovesicovaginal...	8	1		5		1		1†	1		3	2	1	1
Vesicocervical.....	1							1‡			1			
Ureterovaginal.....	14	6			7		2		1	5	8			1
Ureterocervical.....	4				1		2				3			
Ureteroabdominal.....	2				1		1				2			
Total.....	118	29	23	46	9	2	5	4	21	8	73	3	8	5

\* Transvesical closure of fistula.

† Reconstruction of urethra—Farrar technique.

‡ LaForte operation using rectocele to close opening in urethra and bladder. Martius technique for incontinence.

§ Complete hysterectomy. Repair of fistula by transperitoneal route.

nique for this purpose, recently described, has been successful in 9 out of 10 cases operated upon by 3 gynecologists. As a means of relieving urinary stress incontinence, transplantation of fascia should always be combined with vaginal plastic surgery. It should never be used as a substitute for the standard vaginal plastic procedures in use for the same purpose. In all plastic procedures involving the anterior vaginal wall, it is important to separate the wall of the vagina from that of the bladder in the natural plane of cleavage.

The author presents a series of 118 urinary fistulas. Approximately one-third were caused by obstetric trauma, about one-half by surgical trauma, and 15 per cent by malignant neoplasms of the uterus, alone or in combination with irradiation therapy used in treating such tumors. The results of treatment of these 118 cases are summarized in Table II. 4 figures.

(This is a most informative yet simply written paper by an able plastic surgeon in a hospital whose history has been intimately linked up with the development of plastic gynecological surgery. It gives a concise review of methods available for the correction of urinary fistulas as well as of "stress incontinence". The author emphasizes the importance of intensive efforts to close fistulas at the first operation, since failure so commonly means greater difficulties at subsequent attempts. His insistence that in all plastic procedures involving the anterior wall the vagina be separated from the bladder in the natural plane of cleavage will be endorsed by everyone with experience in this field. Aside from anatomical disadvantages, it avoids the more difficult dissection and the far greater vascularity which follows if one gets into the wrong plane. Although the now widely and successfully used method of flap splitting and free mobilization of the bladder has been known for a half century, it took a great many years before it permeated our specialty. It was the common practice among gynecologists of a generation ago to resort to the Sims type of operation, perhaps with many failures before final success, in the closure of the larger fistulas, most of which are now successfully treated by a single operation based on the above mentioned principles.

As regards stress incontinence, the author presents a brief but satisfying review of the simpler techniques, such as that of Kennedy, successfully employed in the great majority of cases. For the smaller group of cases not cured by these conservative plans, Aldridge again calls attention to the operation described by him in 1942, employing a combination of vaginal plastic surgery with transplantation of the abdominal fascia. (*Am. J. Obst. & Gynec.*, 44: 398, 1942). A modification of this plan has recently been suggested by Studdiford (*Am. J. Obst. & Gynec.*, 60: 119, 1945) whose paper was abstracted and commented upon in the February issue of the Survey, p. 134. A number of instructive illustrations accompany Aldridge's article, as well as several tables. One of these, showing the results in the treatment of 118 fistulas, is reproduced above.—Ed.)

## VESICOVAGINAL FISTULA; AN IMPROVEMENT IN THE CHAFFIN METHOD OF POSTOPERATIVE TREATMENT, USING CHAFFIN SUCTION DRAINAGE

R. C. CHAFFIN

*Am. J. Surg.*, 71: 305-311, 1946

The results of surgical treatment of bladder fistulas were unsatisfactory until about the time of the publishing of the author's original article advocating the prone position of the Bradford frame for complete drainage. A review of the literature since that time indicates that surgical results are more universally satisfactory. The position of the patient caused some discomfort and complaint due to the rigidity of the Bradford frame. In the present paper the author has removed the woman from the frame and placed her in bed with still better drainage.

The following is a step-by-step operative technic which yields good exposure and results in an easy operation. The patient is placed in the Trendelenburg (45 degree) position.

1. Two Gelpi retractors are used, one to separate the buttocks at the anal level and the other to spread the vagina.

2. Cover retractor with towels to avoid suture tangles.
3. Sims' retractor in the perineum, is pulled up by a strong assistant. (Usually it is necessary to incise the perineum to the sphincter ani to get good exposure.)
4. Pull down the cervix (if cervix is absent, the scar above the fistula is seized in the tenaculum). This places the surgical site directly in front of the operator with good exposure and an opportunity to work on a flat surface. Lateral retractors aid in exposure.
5. A vertical incision is made over the fistula, one cm. above and below, through the vaginal wall (small tonsil sponges and long tissue forceps are used for sponging).
6. Carry dissection back one cm. in all directions and hold vaginal flaps with long Allis or sutures.
7. Suture the bladder opening with gastrointestinal chromic catgut and curved needle, interrupted.
8. Close vaginal wall with any suture of choice; gut, silk, linen, cotton or wire.
9. Place a small rubber catheter (plain, not Pessar) into the bladder about 2 inches and secure with cotton cord and adhesive.
10. Cut off the catheter at about its middle or fairly close to the perineum, attach by "T" glass connection to a  $\frac{3}{16}$  inch pure gum tubing, sufficiently long to reach over the bed (3 to 4 feet). Attach a small rubber tube to the side arm of the "T" tube and bring up and strap to buttocks with adhesive. This remains open for suction air intake.
11. Place the patient in her bed, not on the Bradford frame, in the prone position. *"This is the point where we remove the patient from the Bradford frame where she has been for ten or fifteen years and make her more comfortable."*

From this point the Chaffin suction technic applies. The long, large catheter extension tube with the "T" tube making a vent for air intake, goes to the Pratt bedside pump which maintains a constant suction of 20 inches of water and is continued for 10 days to 2 weeks. The urine flows out of the bladder to the bed level by gravity. The suction pump picks it up at this point and lifts it over the edge of the bed, or even over the thigh more effectively than the Bradford frame and gravity method, with much greater comfort. The author cautions that suction must not be applied to a closed catheter as it will not empty the bladder without the admission of air.

Suction drainage is applicable to scores of surgical fields and especially fits this pathological entity. Suction drainage lowers mortality in all abdominal surgery, possibly as much as 80 per cent and in ureter and bladder fistulas and transplants, is adequate insurance against failures or complications. 14 figures.

(While there are many possible difficulties and hazards in the operative and postoperative care of bladder fistulas, I doubt whether most gynecologists would class among the major ones the difficulty of keeping the bladder empty after operation. For this purpose the retention catheter is almost universally employed and, like the author, I prefer the plain catheter to one of the mushroom type, because of its lesser traumatic possibilities. While the suction drainage plan described by Chaffin might be an additional safeguard in some of the more difficult and doubtful cases, it would not seem necessary in the average case. The

risk of catheter plugging would probably be less, but not that imposed by slipping out of the catheter. In no other type of gynecological case is the importance of postoperative nursing greater than in the management of fistulas. Fortunately the gynecologist who has a permanent nursing staff well trained in such matters, rather than the constantly shifting nursing personnel on which these responsibilities are more commonly put!—Ed.)

## THE RADIATION TREATMENT OF CARCINOMA OF THE FEMALE URETHRA

J. JACKMAN AND R. D. BACON

Pennsylvania M. J., 49: 518-519, 1946

The purpose of this paper is to report the technic of radiation therapy of carcinoma of the female urethra as used by the authors; to describe the reactions and complications, both early and late, to this method of therapy; and to list the immediate results in a small series of cases observed during the past 5 years.

Most primary urethral malignant tumors are squamous carcinomas. A definite diagnosis depends upon histologic examination of biopsy tissue. After removing adequate tissue for biopsy, the cautery may be used to destroy as much of the lesion as possible. When the diagnosis is established and the tissue has at least partially healed, x-ray therapy may be started. This is administered by a cone adapter with the cone directly against the external meatus, covering all of the diseased area. The following factors are used: 200 kilovolts, 15 milliamperes, Thoraeus filter, 50 cm. focal distance; 300 r (measured in air) are given daily for 5 or 6 days. This is followed immediately by radium element needles, 3 or 4 10 mg. needles being inserted radially around the urethra and parallel to its long axis. For the volume of tissue treated a gamma roentgen dose of 3 to 4 thousand is used, concentration of the dose being attempted around the external meatus. If enlarged nodes are palpable in the inguinal areas, radical dissection is carried out, which may be followed by high voltage roentgen therapy.

Excessive irradiation is not very well tolerated by the urethral area and the leeway between an adequate therapeutic dose and overdosage is small. Telangiectasis and post-irradiation stricture may result.

The authors have treated 8 cases of urethral carcinoma in the past 5 years. Seven of the patients are living and one is dead. Five patients are at present free from symptoms and signs of disease. The 6th, originally treated 5 years ago, although without evidence of local disease is suspected of having distant metastases. The 7th is now being treated for local recurrence, 16 months after the primary treatment. The patient who died presented evidence of inguinal node metastases when first seen; both the urethral primary lesion and the metastases were microscopically proved as squamous cell carcinoma. Treatment consisted of inguinal and urethral dissection as well as x-ray and radium therapy to these areas. Death occurred 7 months later.

Although 5 and possibly 6 of the 8 cases are free of disease for a few months to 5 years after primary treatment, a favorable prognosis cannot be given them until more time has elapsed. It is noted that the presence of metastases to the inguinal lymph nodes is a very unfavorable sign.

(The results in the 8 cases reported by the authors are better, I believe, than those commonly observed. Many of these cases are observed late, and only in the occasional case does surgery, without undesirable loss of sphincter function, find a place in treatment. I have now under my care a huge diffuse urethral carcinoma extending upward into the vesical neck, and forming a large mass almost filling the vagina. The patient had had hematuria for 6 years. Incidentally, urethral carcinoma of this large size may be difficult to distinguish from primarily vaginal growths, although the latter, when they reach considerable size, commonly show ulceration and vegetation on the vaginal surface. Even a large urethral carcinoma, on the other hand, is apt to be covered by a smooth vaginal mucosa. The picture is different with urethral carcinomas in the meatal end, sometimes secondary to caruncles, and characterized by an ulcerated fungoid appearance.—Ed.)

## IS URETERAL STRICTURE AN ETIOLOGICAL FACTOR IN THE GENESIS OF RENAL CANCER?

GUY L. HUNNER

Urol. & Cutan. Rev., 45: 32-57, 1946

The author has found in most instances that cancer of the kidney is associated with bilateral ureteral stricture. From what is known concerning the capital rôle of ureteral stricture in causing hydronephrosis, renal infections, calculus formation and nephritic processes giving rise to the so-called essential hematurias, it seems reasonable to conclude that stricture, with its urinary stasis and renal injuries, is probably one of the chief factors in the development of renal cancer.

If use is made of the methods which reveal stricture and of the logical cystoscopic methods for the relief of this malady, in another quarter-century there should be a great reduction in the incidence of renal cancer.

Every bleeding kidney should be considered as the seat of cancer until reasonable proof is established to the contrary. If the treatment of ureteral stricture results in prompt cessation of hematuria, one is justified in making the diagnosis of probable "essential" hematuria, but the patient should be carefully supervised for a prolonged period. If pain, hematuria and tumor are present, dilatation of ureteral stricture may result in cessation of the pain and hematuria, and, if there is a family history of congenital cystic kidney, one is justified in concluding that the tumor belongs in this category.

When the cancer kidney is not definitely outlined by palpation or routine urograms, a prompt diagnosis may be reached by combining with the urogram an outlining of the kidney with the peri-renal air injection.

When the patient has such profound anemia, toxemia and asthenia that imme-

risk of catheter plugging would probably be less, but not that imposed by slipping out of the catheter. In no other type of gynecological case is the importance of postoperative nursing greater than in the management of fistulas. Fortunate the gynecologist who has a permanent nursing staff well trained in such matters, rather than the constantly shifting nursing personnel on which these responsibilities are more commonly put!—Ed.)

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## OPERATIVE GYNECOLOGY

### VAGINAL HYSTERECTOMY; A RECORD OF RESULTS BASED ON THE WEIR TECHNIQUE

E. E. RHOADS AND P. R. ZEIT

Am. J. Obst. & Gynec., 51: 533-537, 1946

That vaginal hysterectomy is a procedure of inestimable value is hardly debatable. Any so-called routine technique must be modified in each individual case and the description of a number of techniques and their end-results in the hands of various operators is of value in evaluating the operation. Thus, the authors present a description of the technique of Dr. W. H. Weir and the end-results obtained at the University Hospitals of Cleveland.

From 1928 to 1942 there were 6017 hysterectomies performed. Of this total, 3641 were abdominal hysterectomies and 2091 were supracervical hysterectomies. Three hundred and eighty-five vaginal hysterectomies were done, or a percentage of 6.39. Dr. Weir's technique was used in 205 of these cases.

This technique, which the authors describe in the present paper, is felt to have given very satisfactory results. An important feature of the technique is suturing the base of the bladder to a united upper pedicle. In using the suture method, adequate outlet with good exposure is necessary. Plication of the uterosacral ligaments is extremely important to prevent recurrent prolapse and enterocele.

One hundred and ninety-two of the 205 patients have been followed up from 2 to 10 years. The results show a mortality of 1.04 per cent, recurrent rectocele in 2.60 per cent, recurrent cystocele in 3.64 per cent and prolapse of the vaginal vault in 2.08 per cent. There was one pelvic abscess (.52 per cent), shortened vagina in 2.08 per cent, urethrocele in 1.04 per cent, stress incontinence in 2.08 per cent and vesicovaginal fistula in .52 per cent. There were 3 enteroceles, 2 of which were overlooked at operation (1.04 per cent), and one of which was recurrent (.52 per cent). The 2 overlooked enteroceles were corrected satisfactorily by later operation and the vesicovaginal fistula healed spontaneously making a corrected total of 14 unsatisfactory cases, or 7.07 per cent.

Although, according to Danforth, postoperative hemorrhage is a not infrequent occurrence, there was but one in this series requiring secondary operation.

*(Gynecologists all have their little individual tricks and touches, not only in vaginal hysterectomy, but with practically all operations. Instead of "suturing the base of the bladder to a united upper pedicle", many of us prefer to employ a suburethral triangular stitch embracing the combined infundibulo-pelvic ligaments and the subpubic ligament on each side in those cases in which there is an associated large cystocele which calls for repair. Too much stress cannot be put on the obliteration of the cul-de-sac by a purse-string suture embracing the uterosacral ligaments, and this will usually avoid the later development of pelvic enterocele, which is urged by some as an argument against vaginal hysterectomy in prolapse cases. Postoperative hemorrhage of slight amount is not rare, as in most other*

diate operation is out of the question, bilateral opening of the ureters for good drainage often yields surprising results in the improved condition of the patient. In case of doubtful diagnosis, the catheterized bladder urine should be repeatedly examined during the waiting period since it sometimes yields tumor cells, thus clinching the diagnosis.

In the treatment of bilateral stricture in hundreds of patients who had chronic pyelitis or infected stone kidney on one side only, the author has reason to believe that the sterile kidney became infected due to catheterization in no more than 4 or 5 instances. If one does not approve of dilating the supposedly normal ureter before removal of the cancer kidney, he should certainly see that this is done before dismissal of the patient as an insurance for optimal health of the remaining kidney and as prophylaxis against future cancer on that side.

Twelve case reports are presented. 33 figures.

(Howard A. Kelly, who devised the direct method of cystoscopy for women, may be called the father of female urology, and Hunner has been the outstanding exponent in this field for many years. Certainly his discussion on the diagnosis of renal cancer, based as it is on an enormous experience, will be accepted as authoritative. As to the etiological role of ureteral stricture, there will probably be no unanimity of opinion, partly because of differing viewpoints as to the interpretation of strictures, partly because many will feel that stricture is perhaps not the type of "chronic irritative" lesion which is commonly thought to play a predisposing role in cancer development. Dr. Hunner would probably agree that here, as with many other supposedly predisposing factors in the cancer field, the verdict would have to be the old Scotch one of "not proven."—Ed.)

which adenocarcinoma of the corpus was diagnosed 2 years after the performance of a diagnostic curettage and Watkins interposition operation. Following a most difficult complete hysterectomy, the patient made an uneventful recovery. She now has a bladder capacity of 24 ounces with occasional lapses of muscular control.

A number of cases have been reported in which the interposition operation was done without tubal ligation during the childbearing period. Practically all patients aborted or went on to term and cesarean section. However, some of these patients have worn retention catheters from the eighth week on.

A case is discussed in which the patient's complaint was frequency of urination, of such a degree that she was miserable. Three years previously a Watkins operation and sterilization had been performed. Cystoscopic examination revealed a bladder capacity of only 100 cc., markedly elevated bladder floor and congested ureteral orifices. It was concluded that the symptoms were due purely to a mechanical reason by the uterus being pushed beneath the bladder.

The author concludes that the Manchester-Fothergill bladder advancement operation or vaginal hysterectomy should offer enough choice of procedure in cases where the Watkins operation formerly has been used.

(As the author states, the complete Watkins interposition operation has apparently gone into the discard, though we shall probably for some years meet with an occasional instance of undesirable late complications, such as the author describes. While I have personally not encountered adenocarcinoma in an interposed uterus, I would be inclined to believe that radium therapy, applied within the cavity after incising of the uterus through the vagina, would be a better plan than radical operation, which would certainly be difficult. On the other hand, in a case of moderate-sized myomas, with profuse bleeding, in a previously interposed uterus, the removal of the latter through the vagina proved rather surprisingly easy, though under such conditions one must be on the guard against bladder injury. Certainly there would be no justification for performing the complete interposition in child-bearing women without tubal sterilization, nor would there be any need for such interposition in view of the availability of simpler and safer methods.—Ed.)

extensive vaginal procedures, but serious hemorrhage should certainly be uncommon if hemostasis has been carefully carried out.—Ed.)

## HYSTERECTOMY; INDICATIONS FOR THE VARIOUS TYPES OF OPERATION

DAVID A. BICKEL

J. Indiana M. A., 39: 110-112, 1946

The author reviews a small group of personal cases and also statistics on hysterectomy operations from large teaching clinics and general hospitals. These studies indicate that the trend in pelvic surgery is to remove the entire uterus when hysterectomy is performed, and to do the operation vaginally when conditions permit.

From the standpoint of operative technique and safety, some operators prefer the subtotal operation, and also prefer it in cases of extensive pelvic inflammation or endometriosis. Because of the danger of the development of malignancy and the persistence of chronic infection in the cervical stump, the total operation should be the operation of choice for those familiar with pelvic surgery. If a diseased cervix is not removed it should be thoroughly treated pre- or post-operatively and examined at regular intervals.

Vaginal hysterectomy definitely is becoming the choice operation for the correction of uterine prolapse and removal of the uterus in the same procedure.

(A brief summarizing paper which, I believe, states present trends correctly.—Ed.)

## LATE COMPLICATIONS OF THE WATKINS INTERPOSITION OPERATION

CLAYTON T. BEECHAM

Am. J. Obst. & Gynec., 51: 416-419, 1946

The author states his impression that today the ordinary bladder advancement, the Manchester-Fothergill operation, and vaginal hysterectomy are gradually replacing the Watkins interposition operation. This is probably due to the Watkins operation causing a distortion of pelvic anatomy. The complications of the Watkins operation which are cited in this paper have come under the author's care, although the operations were done elsewhere.

McGlinn, in 1927, reported a case of carcinoma of the uterine body occurring 2 years after a Watkins operation. Bissel stated that he had encountered 2 such cases while Corvese added another report. The author presents a fifth case in

## WHAT IS NORMAL SEMEN?

SHERWIN A. KAUFMAN

Human Fertil., 2: 3-11, 1946

Complete semen analysis in a group of 40 men of repeatedly proved fertility is presented by the author as a preliminary report. The only consistent finding in this series was a high percentage of normal morphological forms in every case.

The wives of the men studied were all pregnant at the time of study, now have 2 or more normal children, and have never had a spontaneous miscarriage. By means of a questionnaire, further evidence of high fertility has been ascertained in 31 of the cases.

The age of the men appeared not to influence the results in any manner. The ages varied from 27 to 54 years, the average being 37.0 years.

The volume of the ejaculate averaged 3.0 cc. No direct correlation was noted between the volume and the sperm count per cc.

No constant relationship was seen between viscosity or turbidity, and any other phase of the analysis.

Motility estimations revealed an average of 61 per cent motile cells at the end of 3 hours. At the end of 6 hours, the motility averaged 46 per cent and at the end of 12 hours the average was 2.8 per cent motile forms. Three specimens showed definitely poor motility, including poor quality of motion, and 2 of these had a markedly reduced spermatozoan count.

The spermatozoa count per cubic centimeter was less than 60,000,000 in 6 of the 40 cases. Two cases had counts less than 40,000,000 per cc. The average count for all cases was 107,100,000 per cc.

The average total count was 332,000,000. Seven specimens had total counts below 150,000,000, and 5 of these had counts below 60,000,000 per cc.

In the study of morphology, the average percentage of normal forms was 89.4 per cent. Abnormal forms ranged from 3.0 per cent to 18 per cent with an average incidence of 10.6 per cent. In no case did the percentage of abnormal cells exceed 18 per cent.

(The plan of study followed in this paper is somewhat similar to that employed some years ago by Hotchkiss and his co-workers in that the men chosen for semen studies were those of demonstrated fertility. Surprisingly low counts were reported in some of Hotchkiss' cases, counts far below the 60 million minimum limit for fertility which was at one time set. In a number of Kaufman's cases also the count was well below this figure, and there is no doubt that still lower counts characterize the semen of some unquestionably fertile men. The morphology would seem to be a more reliable index, as investigators appear to be in pretty general agreement that a high percentage of abnormal forms, above 20 per cent, is quite sure to mean infertility.—Ed.)

## STERILITY

### HUMAN FERTILITY

C. SCOTT RUSSELL

Lancet, 1: 300-303, 1946

According to Pearl "the relative sterility of the human organism is truly the marvel rather than fertility." This conclusion is based on the study of 199 couples who must have taken on the average about 24 months to conceive. Because clinical experience in the author's country does not support this view, a short investigation was carried out with the main object of obtaining an estimate of the time taken to conceive.

Records of 197 first conceptions and 96 second conceptions were available and were analyzed for this study. Details of third and subsequent conceptions were not recorded. It was found that nearly two-thirds of the pregnancies started within 3 months of natural coitus. This finding does not, therefore, confirm Pearl's conclusion.

A trend was apparent suggesting that second babies are conceived slightly more easily than first babies.

Two-thirds of the women interviewed had practised birth control before the first conception, and the same proportion had practised it between the first and second conceptions. Coitus interruptus was the usual method of birth control. The duration of successful contraception was significantly shorter in couples who had not conceived than in those who had conceived at once. The failure of birth control was significantly greater between the first and second conceptions than before the first. The explanation may be either the longer duration of contraceptive effort or the increased use of coitus interruptus at that time. No significant difference was demonstrated between the ease of conception in women who previously had and those who previously had not practised birth control.

The author criticizes Pearl's data from the following 2 points of view: (1) the statement that his group of 199 couples is "reasonably representative" is questioned, and (2) it is suggested that his method of obtaining accurate information about the practice of birth control was so unsatisfactory that much of his data on this subject must be viewed with suspicion.

(While Raymond Pearl was a distinguished statistician, the conclusions reached by Russell will probably impress most gynecologists as more in keeping with actual experience than Pearl's.—Ed.)

husband's infertility, the wife, with her husband's consent, submits to artificial insemination by a donor other than her husband. It may also happen that she resorts to such a procedure without her husband's consent or knowledge. Such a case was presented to the Ontario (Canada) Supreme Court in 1921.

The parties were married in Canada and, shortly thereafter, sailed for England. The husband returned to Canada and the wife remained in England for several years, during which time she submitted to artificial insemination without her husband's knowledge, the semen specimen being provided by another man. She returned to Canada with the child and sued her husband for divorce and alimony, charging that his neglect and cruelty drove her to the act described. The court held that the wife's submission to artificial insemination (by another man, without her husband's consent) was adultery, the essence of which was not necessarily the moral turpitude involved, but the surrender of the reproductive powers of the wife to another man. The court said: "Sexual intercourse is adulterous because in the case of the woman it involves the possibility of introducing into the family of the husband a false strain of blood. Any act on the part of the wife which does that would, therefore, be adulterous."

The author concludes that if the wife submits to artificial insemination without her husband's knowledge or consent, the offspring thus produced is illegitimate.

The real field for the application of artificial insemination is when the wife is fertile and the husband sterile and when, because of their mutual desire for a child, the husband consents to the procedure. The question of legitimacy under these circumstances was the subject of an editorial in the *American Medical Association Journal*, which took the view that the child is illegitimate. In this editorial it was pointed out that the husband's consent does not alter the fundamental concept of legitimacy, which requires that the child be the actual offspring of husband and wife. If that concept is violated, even with the best of intentions, the resulting offspring is illegitimate.

(In the case reported by Schatkin, where the insemination was done without the knowledge or consent of the husband, the verdict of illegitimacy rendered by the court is not surprising. More important is the fact that even with the full knowledge and consent of the husband, the question of the legitimacy of the child may still be brought up, and, if this viewpoint is presented to the prospective patient, as it should be, her enthusiasm for the procedure will probably be much dampened. She is likely to choose adoption instead. While I suppose that there is justification for occasional resort to insemination, it is a rather disagreeable, messy procedure, with very definite legal connotations. In every large community there are likely to be a few enthusiasts for the method, and I am always glad to refer seekers for "testtube babies" to them.—Ed.)

## THE LEGITIMACY OF ARTIFICIAL INSEMINATION

ALAN F. GUTTMACHER

Human Fertil., 2: 16-17, 1946

In general, legal interpretation is resistant to the passage of time and to the associated changes in social attitudes. None of the legal opinions referred to by

## THE RELATION OF HYALURONIDASE IN THE SEMINAL FLUID TO FERTILITY

B. E. GREENBERG AND S. L. GARGKILL

Human Fertil., 2: 1-2, 1946

It has been suggested that hyaluronidase may be the enzyme which is responsible for the dissolution of the corona of the ovum which thus allows the sperm easier penetration. The present paper concerns the relationship of the concentration of spermatozoa to the amount of hyaluronidase present in a sperm specimen.

Hyaluronidase is an enzyme which decreases the viscosity of solutions containing hyaluronic acid. The authors chose the umbilical cord of the new-born as a good source of supply of hyaluronic acid. A special viscosimeter was set up for measuring the action of hyaluronidase from the spermatic fluid. The general findings were that the concentration of hyaluronidase in spermatic fluid is in direct proportion to the number of spermatozoa found in a given specimen.

Such findings provide an opportunity for an additional check on possible errors in the count of spermatozoa and they offer a probable explanation why, when there is not enough hyaluronidase in the spermatic fluid for the dissolution of the egg of the corona, no pregnancies take place, even though a small number of good motile spermatozoa is found.

It was found that the spermatozoa do not carry hyaluronidase but that it is present in the spermatic fluid itself. If hyaluronidase is essential for the dissolution of the corona and if spermatozoa do not carry hyaluronidase, it was assumed that there must be some other mechanism of transportation of the seminal fluid and spermatozoa in addition to the passage of the individual spermatozoa up into the cervix and tubes.

On this assumption, the authors established the fact that no hyaluronidase is present in the normal tubes of a female rabbit. Then they copulated rabbits, killing the female within 30 seconds after copulation. The Fallopian tubes were removed and the presence of hyaluronidase was definitely established. It is concluded that in all probability there is some mechanism of suction which causes the sperm fluid to appear in the tubes of animals.

## ARTIFICIAL INSEMINATION AND ILLEGITIMACY

SIDNEY B. SCHATKIN

Human Fertil., 2: 14-16, 1946

If husband and wife are both fertile, yet the latter cannot conceive due to the difficulty or impossibility of normal sex relations, resort may be had to artificial insemination with the husband as donor. There can be no question of the legitimacy of the offspring thus created. However, it may be that due to the

## MISCELLANEOUS

### "HYPERTRICHOSIS IN THE YOUNG WOMAN—ONE HUNDRED CASES. INFLUENCE OF THE HYPOADRENALISM"

ENRIQUE CANTILLO AND MARTIN CALVO

Anales del Ateneo del Instituto de Maternidad y Asistencia Social, Buenos Aires, 195-200, 1945

The authors report studies made on 100 cases of so-called hypertrichosis of the feminine type in young women between adolescence and menopause. This form of hypertrichosis ought to be distinguished from the viriloid hirsutism seen at the menopause.

The symptomatology seems to indicate that the cause of this syndrome lies in a deficiency of the ovarian-adrenal functional synergism. Besides the hypertrichosis, such patients also complain of weakness, easy fatigue, psychic depression, anorexia, vagotonic symptoms, cephalalgias, disturbances in pigmentation, menstrual disorders (usually amenorrhea or hypomenorrhea and occasionally metrorrhagia). The blood pressure is frequently low (both systolic and diastolic), the basal metabolism varies from minus 10% to minus 20% in the majority of cases, and the sugar tolerance is rather high.

According to its etiology, the authors believe that treatment should be based on the administration of pluriglandular products not containing pituitary principles, but, on the other hand, rich in ovarian hormones. Results of treatment are not reported.

(Hypertrichosis is one of the most distressing of feminine problems, especially when it involves the face. Aside from the rare cases in which it is part of the syndromes produced by removable endocrine tumors, such as arrhenoblastoma, adrenal tumors of the ovary, or certain cortical lesions, no known method of hormone therapy seems to be of avail. The authors of the above paper do not report their results, and one can be sure that they were poor after the methods of treatment they advise. I have seen no good results from the use of estrogens, which so many have advised, nor do there seem to be any worthwhile results reported by others.

The chief measures in treatment are psychological and cosmetic. Many of these patients look upon hirsutism as evidence of masculinization, which it usually is not, for it is often seen in patients who otherwise are typically feminine, with normal menstruation, normal fertility, normal breast development and the normal psychology of the female. They need reassurance and enlightenment, for they are morbidly self-conscious of their affliction. Modern cosmetic methods will do much to alleviate this unfortunate problem, and the better class of beauty shops are a boon. In the milder cases, electrolysis can be resorted to, while in others bleaching of light hairy overgrowth makes it much less conspicuous. In the more marked cases paraffin depilatories keep the situation under control, but in the extreme cases frequent shaving is necessary. Various adjuvants to the latter, such as the rubbing in of powdered pumice, are also of value.—Ed.)

Mr. Schatkin places in proper focus 3 imperative facts: first, the intent; second, that artificial insemination is done with the husband's full knowledge and consent; and third, that it is a procedure utterly devoid of any carnal or sexual contact.

Carrying out the legal premise that "sexual intercourse is adulterous because in the case of the woman it involves the possibility of introducing into the family of the husband a false strain of blood," a hysterectomy would be 100 per cent protection against the possibility of committing adultery. Certainly if the woman without a uterus has extra-marital coitus she could not contaminate her husband's blood line; therefore, logically she would not be an adulteress. From the physician's point of view, it is the intent which is all important.

The fact that the husband agrees to artificial insemination is a very important matter. The author will never undertake a case of artificial insemination unless he has had a careful discussion with the husband and is fully assured of his sincere desire for this solution to their sterility problem.

Furthermore, from the physician's point of view, the fact that artificial insemination is an asexual method of impregnation is extremely important.

The author concludes: "I honestly believe that if artificial insemination were presented to a liberal court, a bench made up of nine Oliver Wendell Holmeses, its legitimacy would be affirmed. Some day it will be."

(See comment on preceding paper. Guttmacher's remarks on Schatkin's paper would seem to have no bearing on the actual legal status of the problem regardless of the fullest and most willing cooperation of the husband. This is particularly true since we do not have, nor are we likely to have in the foreseeable future, "a bench made up of nine Oliver Wendell Holmeses." While it has nothing to do with the immediate matter of artificial insemination, I should like to relate a rather recent experience illustrating the extreme lengths to which some childless women will go in their desire for babies. I was consulted by a highly intelligent woman whose problem was sterility, and the study soon revealed that this was due to the male factor, her husband having a complete azoospermia. The wife was told of this, but she declared she would not tell her husband, because she feared it would be a tremendous blow to him. "But," she said, "I'm going to have a baby, because I believe it would make my husband the happiest of men, and I'll have it through intercourse with some other man." I told her I could not make myself her moral mentor, but I warned her that a single coitus is often unsuccessful, adding jokingly that if repeated she might become an addict. However, she insisted that she loved only her husband and was making the sacrifice for his sake and for purely (sic!) procreational purposes. Before many months she returned beaming with excitement because she had skipped a menstrual period, and soon there was no doubt of pregnancy. She was as happy as a woman could be, and hence I was shocked a month or two later to read a newspaper account of her suicide. Although I surmised what might have happened, it was not until some time later that I learned from a member of her family that, without his wife's knowledge, the husband had had several previous examinations establishing his absolute sterility. When his wife informed him of her pregnancy, angry accusations of adultery were heaped upon her, with threats of divorce, and then followed the tragic sequel of the wife's extramarital insemination.—Ed.)

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## EARLY HISTORY OF THE HUMAN GERM CELLS

E. WITSCHI

Anat. Rec., 94: 506-507, 1946

About fifty well-preserved human embryos and fetuses from the Carnegie and the Iowa collections were studied to trace the prenatal history of human germ cells. A series of twenty-four represent the period during which the primordial gonia migrate from the yolk sac epithelium to the sex gland primordia (12 somite to 8 mm. stages). Progressing with ameboid movements, the cells apparently pass through membranes and other obstacles by lytic destruction. During the entire migratory period they continue to multiply, their number increasing from about 100 to near 2,000. This indicates an average of four to five mitotic sequences for this interval of approximately 12 days.

At the site of the gonad primordia, the germ cells become individually encapsulated with follicle cells which are probably derived from the coelomic epithelium of this region. With ovarian differentiation they become the granulosa cells; in the testicular direction they form sustentacular cells. In female fetuses of 11 weeks (60 mm.), some ovogonia have entered the synaptic phase, thus becoming ovocytes. Three weeks later (93 mm. fetus) the ovocytes prevail and ovogonial multiplication seems near its end. An estimate based on germ cell counts in definite parts of the sectioned ovaries puts the number of germ cells for this fetus in the neighborhood of five million. Since follicular atresia starts early, this number decreases even before birth.

(This study furnishes additional evidence in support of the view that the germ cells do not arise from the germinal epithelium, as was formerly commonly believed, but that they migrate to the gonadal anlage from a much earlier situs in the epithelium of the hindgut. The correctness of this *Keimbahn* concept has apparently been well established in the case of some of the lower animal forms, and there is increasing evidence, such as that presented by Witschi, that it also applies to the human.—Ed.)

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# *Obstetrics*

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## PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

### VITAMIN E LEVELS IN MATERNAL AND FETAL BLOOD PLASMA

J. V. STRAUMFJORD AND MARY LOUISE QUAIFFE

Proc. Soc. Exper. Biol. & Med., 61: 369-371, 1946

Plasma for these studies was obtained from oxalated blood from the cubital veins of women and from oxalated blood from [the placental end of the newly cut umbilical cord before delivery of the placenta. Samples from mothers were obtained immediately after delivery—about  $\frac{1}{2}$  hour later than the cord samples. Vitamin E levels were determined by the method of Quaife and Harris. Briefly, the method comprises extraction of plasma lipids with ethanol and petroleum ether, hydrogenation to obviate interference due to carotenoids and vitamin A, and application of the Emmerie and Engel color reaction to measure total tocopherols (vitamin E).

Plasma vitamin E values were determined on 23 women in various stages of pregnancy. The results showed an increased level of tocopherols in the latter part of pregnancy; 11 women in the first 24 weeks of pregnancy had a mean level of 1.17 mg. % tocopherols and 12 patients in the 25th to 36th week of pregnancy had a mean level of 1.62 mg. %. Mean levels of plasma vitamin E for men and non-pregnant women have been found to be 1.05 mg. % and 10.4 mg. %.

Plasma vitamin E values were determined on 54 mothers and respective cord bloods at delivery. The mean maternal vitamin E was 1.70 and the mean fetal vitamin E was 0.34. The mean ratio of plasma vitamin E in the mother to that in the infant was 5.7. Thus, vitamin E is similar to other fat-soluble vitamins in showing markedly lower values in the infant than in the mother. The correlation coefficient of maternal and fetal vitamin E levels showed absolutely no correlation between the 2.

There was no statistically significant difference between the plasma vitamin E levels in male and female infants. There was no correlation between vitamin E in the infant and birth-weight.

It has been shown that the blood lipids increase in pregnancy. Vitamin E accordingly behaves in a similar way. The concentration of lipids in the fetal plasma is generally much lower than in the maternal plasma which is likewise true of vitamin E. This relationship has been shown to hold also for vitamin K as

measured by prothrombin levels. While this placental barrier may be regarded usually as a protective mechanism, it is possible that it does not always function in a beneficial way. Administration of supplements of vitamin E to the mother during pregnancy might possibly increase the fetal plasma vitamin E. Experiments to test this point are in progress.

## THE INACTIVATION OF PLACENTAL TOXIN BY HUMAN SERUM

CHARLES L. SCHNEIDER

Am. J. Physiol., 146: 140-145, 1946

A toxic principle which can be extracted from pregnant uteri is rapidly inactivated by blood *in vitro* and *in vivo*, and if sufficiently small amounts of serum are added, only partial inactivation of the toxin occurs. The present investigation is an attempt to work out a method for the measurement of the inactivating potency of serum. Certain properties of the inactivating system have been studied, and these are presented, together with their implications for the measurement of the inactivating potency.

Determination of the inactivating potency of serum is made by measuring the percentage of toxin inactivated during treatment with serum. The percentage inactivation of the toxin is determined with the mouse assay. In this assay the unit of toxin is the minimum lethal dose on intravenous injection into a 20 gram mouse. The toxin is inactivated by the serum from animals of either sex. In the present study the serum was procured from pregnant women, either during or shortly after labor. The toxin was extracted from dried human placenta.

Results showed that the inactivation of the placental toxin by small amounts of serum came to an end point at which some of the toxicity still remained. The reaction between the toxin and the serum inactivating system was not stoichiometric. The inactivating system itself appeared to be gradually inactivated or inhibited. The relation between concentration of serum and amount of toxin inactivated was approximately logarithmic. One unit of inactivating potency is defined as that amount which will inactivate a toxic placental extract to half strength under the prescribed conditions.

The toxicity of the extracts of the dried placenta was similar to that previously reported for extracts of fresh placenta; that is, the injection of the extracts was lethal to mice and sub-lethal doses resulted in focal liver necrosis.

The author postulates that since the toxic extracts of placenta and of endometrium have been found to have certain properties, and since other investigators have shown that toxic extracts of pseudo-pregnant rabbit uteri are inactivated by histaminase, it may be that the inactivating system of serum studied here is histaminase (diamine-oxidase). That histaminase is not specific to histamine

alone, but oxidatively de-aminates any diamine having a free amino group is consistent with the conclusion of other investigators. The toxin of placental extracts is probably not histamine, since it is heat labile and does not pass a cellophane membrane.

That diamine-oxidase is inhibited by several substances and inactivated by others suggests a possible basis for the decreasing potency of the serum during the reaction in the present experiments. The possibility is not excluded that the inactivation may be brought about by an antibody reaction.

## THE DURATION OF GESTATION; WITH SPECIAL REFERENCE TO THE CALCULATION OF THE DATE OF DELIVERY FROM BASAL TEMPERATURE GRAPHS

PENDLETON TOMPKINS

*Am. J. Obst. & Gynec.*, 51: 876-879, 1946

Until recent years there have been but 2 ways to calculate the probable date of delivery. One is to add 280 days to the date of the last menstrual period, and the other is to reckon the duration of gestation from a single coitus, if intercourse took place infrequently and on known dates. The first method is subjected to several errors, it being possible that the patient remembers incorrectly, falsifies the date of her last period, or mistakes "implantation bleeding" for menstruation. Most important, this method of calculation is based on the assumption that ovulation took place 14 days after the beginning of the last period, when it may actually have occurred many weeks after menstruation, a circumstance which could explain cases of "prolonged gestation" which have been reported. The method of calculating from a single coitus is obviously based on the patient's reports and is not an objective means of determining the date of ovulation and fertilization.

Such objective evidence is available in the form of basal body temperature charts. When these are available, one may determine the interval between ovulation and delivery by counting the days; the period of gestation is theoretically 266 days, or 38 weeks. The author presents the graphs of 4 patients in whom the period of amenorrhea exceeded 290 days. In each instance the patient felt that the baby was long overdue. Reference to the graphs shows that each of these patients ovulated more than 2 weeks after menstruation, and that by adding 266 days to the date of ovulation as determined by the temperature graph, none of these patients was significantly overdue.

Thus far, the author's observations, using the temperature graph as an index of ovulation from which to calculate the duration of gestation, have been in agreement with the idea that the normal duration of gestation is 38 weeks. 2 figures.

## A SIMPLE METHOD OF RECORDING UTERINE MOTILITY IN VIVO

B. N. CRAVER, PATRICIA SEIP AND ANNE CAMERON

Federation Proc., 5: 172, 1946

A uterine horn of a rabbit or cat is exposed by an abdominal incision paralleling the course of the horn with the anesthetized animal in the supine position. The horn is brought out through the incision. Two short superficial sutures are so placed in the longitudinal axis of the horn, 180 degrees in the transverse circumference from the point of suspension in the broad ligament, that they are equidistant from their respective ends of the horn and include between them approximately half of the free length of the horn. These sutures are then used to anchor the horn to the abdominal musculature on opposite sides of the incision. A thread is then looped under the midpoint of the portion of the horn included between the 2 anchoring sutures. The thread is then pulled up through a small inverted funnel, fitted with a short stem of comparatively large diameter, and fastened to a recording lever; the funnel serves as a moist-chamber. In such a preparation the blood pressure and respiratory movements may be simultaneously recorded. This preparation permits repeated studies of uterine motility in the same animal if asepsis be maintained and a week to 10 days be allowed for healing, but if a carotid cannula be used for recording blood pressure, only 2 experiments are feasible. The actions of pituitrin, and various salts of epinephrine, histamine, pyribenzamine, prisco (benzylimidazoline), trasentine and atropine in such preparation are reported.

## THE IRRITABILITY OF THE HUMAN UTERUS AS AFFECTED BY VARIOUS DRUGS

G. P. CHILD, R. A. WOODBURY, R. TORPIN, W. G. WATSON AND  
LOUISE JARBOE

Federation Proc., 5: 171, 1946

Human uterine and cervical pressures and electroutero grams were recorded simultaneously. Dysmenorrhea patients were very sensitive to pitressin, 0.2 vasopressor unit of pitressin having a greater oxytocic activity than 0.2 oxytocic unit of pitocin. These patients were also very sensitive to uterine distension; some patients could tolerate a uterine distention of only 2 cc.

The spontaneous activity and the response to pitressin and distension were recorded before and after the administration of various sympathomimetic drugs, parasympatholytic drugs, magnesium salts, calcium salts, barbiturates, quinidine and opiates.

Uterine irritability was reduced by ephedrine, slow injection of epinephrine,

beta-diethylaminoethyl phenyl-alpha-thienylglycolate hydrochloride (Stearns 600), beta-diethylaminoethyl phenyl-alpha-thienylacetate hydrochloride (Stearns 606), magnesium sulfate intravenously, and morphine. In some patients calcium salts and pitocin reduced uterine pain by converting disorganized uterine activity into organized contractions. In other patients some of the drugs had a more pronounced effect in reducing the pain without any marked alteration of the contraction pattern.

## NON-ESSENTIALITY OF HYPOPHYSIS FOR MAINTENANCE OF PREGNANCY IN RHESUS MONKEYS

PHILIP E. SMITH

Anat. Rec., 94: 497, 1946

Thirteen pregnant rhesus monkeys have been hypophysectomized. The complete removal of the anterior and posterior lobes has been confirmed by examination of serial sections of the hypophyseal region. In the five animals examined the absence of pharyngeal hypophysis was established.

In one of the thirteen animals the stage of pregnancy was unknown but at autopsy 21 days after hypophysectomy a living 5 cm. C-R fetus was present. The remaining animals were hypophysectomized at 32, 40, 41, 47, 50, 74, 78, 98, 102, 106, 155 and  $156 \pm 3$  or 4 days (dated from day 13 of the cycle). Six of the animals had normal babies although labor was prolonged, cesarean operations being done in three. The six which went through pregnancy were hypophysectomized on day 32, 50, 74, 78, 102 and  $106 \pm 3$ . The duration of pregnancy after operation was 131 to 50 days. Gestation periods ranged from 159 to 186 days. No milk was secreted.

Of the animals which aborted four had pneumonia, including one hypophysectomized on day 155 of pregnancy. One hypophysectomized on day 41 and one on day 156 aborted, although in fair condition.

The bearing of the author's results on the conjecture that in women prolonged difficult labor may cause destruction of the hypophysis is discussed.

## ON A HUMAN BLASTULA RECOVERED FROM THE UTERINE CAVITY 4 DAYS AFTER OVULATION

A. T. HERTIG AND J. ROCK

Anat. Rec., 94: 469, 1946

The specimen was recovered from a uterus removed surgically on the twenty-first day of a menstrual cycle previously ranging from 25 to 32 days duration.

Probable fertile coitus occurred  $4\frac{1}{2}$  days previously. Endometrium morphologically was characteristic of the eighteenth day, ovulation having occurred 4 days previously. The stigma of the recent corpus luteum was unhealed.

The free-lying blastula was obtained in Locke's solution removed by pipette from the cavity of a submerged uterus opened completely at one side and partially across the fundus. The specimen was discovered with a binocular dissecting microscope using 10 diameters of magnification. Fresh, the specimen measured  $190 \times 150$  micra but after fixation in Bouin's fluid, begun 1 hour after removal of the uterus, it measured  $175 \times 124$  micra. It was surrounded by a sticky, thick, transparent, refractile vitelline membrane which shrank during fixation.

Following dehydration and embedding in celloidin-paraffine, 15 perfect serial sections of 6 micra each were obtained by Dr. Chester Heuser. Nine blastomeres of varying size and shape were present: 5 containing 1 nucleus each, 3 with 2 nuclei each and 1 with 3 nuclei. Three of the single-nucleated blastomeres are in varying stages of mitosis. A segmentation cavity is just beginning to form.

Because of the presence of multinucleated blastomeres the specimen is probably not normal, although no other human specimen is available for comparison.

# MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

## WEIGHT CONTROL, DIET AND FLUID BALANCE IN PREGNANCY

CHARLES H. LOUGHRAN

*Am. J. Obst. & Gynec.*, 52: 42-53, 1946

In the belief that excessive weight gain is a cause of long, hard labors as well as of toxemia, and in an effort to promote the comfort of his patients in pregnancy and afford a prompt return to their previous physical status thereafter, the author has enforced a strict dietary regime on 325 consecutive private patients. In the beginning the weight allowance was 20 pounds, but later it was reduced to 15 pounds as the top weight gain for the average woman; however, the larger the woman the less was the gain permitted and for the unfortunate obese, the ideal sought was no gain whatsoever.

After the general instructions to the patient as to what is expected of her and the results that she may expect from complete cooperation, she is given the usual complete medical and obstetric examination. The proper diet is stressed and she is told how to provide herself with the proper food intake. Here, this means a high protein diet, that is, protein ingested three times a day, which is supplemented by a diet that is low in carbohydrate, high in green and yellow vegetables, fruit, and certified milk, either skimmed or whole, as the diet indicates. In this way, sufficient protein is ingested, sufficient vitamins and salts are included, and carbohydrate is provided in sufficient amount through the ingestion of the vegetables and fruit. All of the heavy starches are absolutely eliminated until we find just what the woman's food requirement is. This must be determined because many women can eat enormous quantities of food in the nonpregnant state without gaining a pound, but pregnancy produces a tremendous gain which must be controlled. Added vitamins are provided and, by frequent office visits, her weight is maintained so that in her first four or five months she is permitted only a maximum gain of one-fourth pound per week, and if she is obese, she is permitted no gain at all.

This early diet regulation is important because in the latter months of pregnancy, as the woman becomes more sedentary, she is apt to put on excessive weight. This is not readily controlled because the restriction in diet has not been started early enough. The patient is seen at least every three weeks at first and, if she is a diet problem, every week until she strikes a proper average. These patients, if gaining beyond their allowance, are put on a 1,200 calorie diet plus added vitamins, which is almost exclusively protein and largely vegetable. More food is later added, and her total caloric requirement found so that she will gain the allowed progressive amount.

Salt is not restricted in the early months, except the ingestion of highly seasoned things, and the excessive use of salt is forbidden. Later, salt is per-

mitted only in the preparation of food. Fluids are important. The woman who can metabolize water is, of course, the usual type. In pregnancy, however, women's water metabolism is notoriously unsatisfactory, and patients are repeatedly checked as to the amount of fluid they take against the amount of urine they excrete. If there is a sudden weight gain the fluid balance is checked. This is done especially in the woman who has been gaining satisfactorily and suddenly shows a pound or more gain, with or without transient edema. This means that she must at intervals measure her intake and output. Her fluid intake is restricted to her previous day's output. The salt is withdrawn and, if her fluid intake and output does not satisfactorily balance, she is instructed to take magnesium sulfate every morning to produce fluid evacuation. Loughan has never seen any harm from this procedure, and these patients themselves remark how well they feel. It is surprising the amount of fluid these patients can lose, as evidenced by weight loss. Their intake is then increased, and if they are able to metabolize a fair amount of fluid, it is allowed, and a balance struck which seems to be best for them. It is also amazing how comfortable they are, how the lassitude disappears, and, what is more important, how often they will ask to be put back on this routine because they feel so much better. In passing, no patient is allowed to take less than 20 ounces of fluid a day. This, of course, does not mean water allowance alone, but means water in any form, such as tea, soup, milk, or other liquid.

One thing we must always watch for carefully is edema, which becomes marked or persistent in spite of this routine. Patients with edema usually belong in either one of two groups: they either eat little protein, or they are heavy protein eaters when not pregnant, and require a great deal more when gravid. Either one of these may get a simple nutritional edema which is alarming unless properly evaluated; also, this may be the first evidence of liver dysfunction. This type of patient persists in having edema beyond a few days, which is not markedly relieved by dehydration. She balances well and has no other evidence of damage; for example, rise in blood pressure, or albuminuria. These patients are hospitalized to make sure that they are maintaining the proper regimen. Almost invariably we find a severe hypoproteinemia. The serum-albumin and serum-globulin ratio is reserved and the serum-albumin is below two. These patients, of course, are headed for trouble. It is not known at this stage, whether their hypoproteinemia is an evidence of liver damage or dysfunction, and is thus an early stage of toxic disease, or whether it is simply some type of nutritional or idiopathic edema, but it calls for immediate control. These patients are put on a very high protein diet supplemented with hydrolysate of protein, and are given an infusion of whole plasma (500 cc.) by vein. This is not the ordinary plasma which is used in shock. Our blood bank prepares this pooled plasma just for this purpose. In ordinary plasma for shock therapy, the 500 cc. is made up of 250 cc. of ordinary pooled plasma and 250 cc. of saline. In this instance there is no saline added, and the whole 500 cc. is pure plasma. It is remarkable how quickly the edema lessens, the weight decreases, and the woman voids an appreciably increased amount of urine. None has required a second transfusion

nor any further treatment, except a continuation of balance. Amigen is not used. It is, of course, ideal in that it includes all the amino acids necessary for growth and development, but amigen in its present state can be given only in solution, and requires 1,000 cc. of fluid to administer its protein. We are afraid of fluid in these cases.

In the author's 325 cases under the above regime there were only two that reached the delivery stage and the delivery room with edema; one was a chronic nephritic, and the other a cardiac patient. There were in the whole group only 32 cases that showed even the slightest transient edema throughout the antenatal period. It might be well here to state that we believe the onset of "toxemia" is concerned

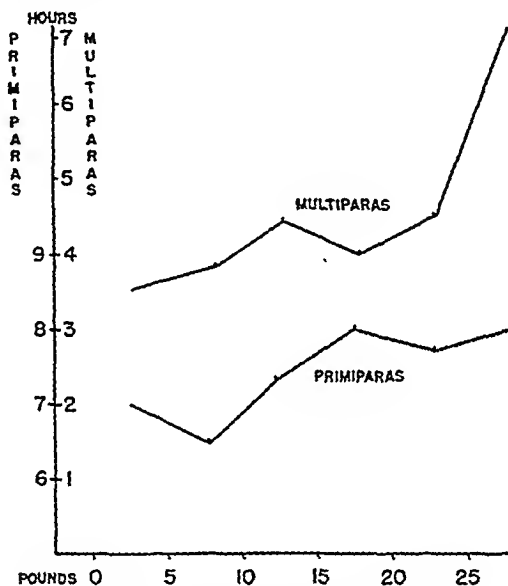


CHART 1. EFFECT OF WEIGHT GAIN, DIET AND FLUID BALANCE ON LENGTH OF LABOR (LOUGHRAN)

with improper water metabolism. The general statistics of the hospital show conclusively the effect of this effort in the reduction of true, pure "toxemia." They show also the total abolition of eclampsia since 1936, where this routine has been used. The only exception was a postpartum eclampsia in which restriction was accidentally discontinued on delivery of the patient. There has not been a death from eclampsia since 1936, and only one since 1933 and, in this instance the treatment was not used. There were in this group of 325, 27 cases that exhibited a transient blood pressure rise of 20 mm. or more, five of these being over 30 mm. and one over 40 mm., but none of these reached the hospital with anything but a normal reading. These transient raises would be ordinarily disregarded, but they were the nearest approach to pre-eclampsia that was observed. The absence of albuminuria was remarkable. In these cases we were able to find only nine specimens that showed an appreciable amount of albumin.

In addition to the beneficial prophylactic effect on toxemia, Loughran is convinced that these patients had easier, more rapid and less complicated labors. The overall gain of all patients was only 14.9 pounds, the primiparas averaging 15.4 and the multiparas averaging 14.3 pounds. The average labor of the group was 6 hours and 17 minutes, primiparas being 7.19 and the multiparas 5.15 hours. The babies in this series were all average in size. There was no baby that was abnormally small and there was none extremely large. There were no fetal deaths from dystocia. The direct relationship between weight gain and dystocia in this series is shown in the accompanying two charts reproduced from the original article.

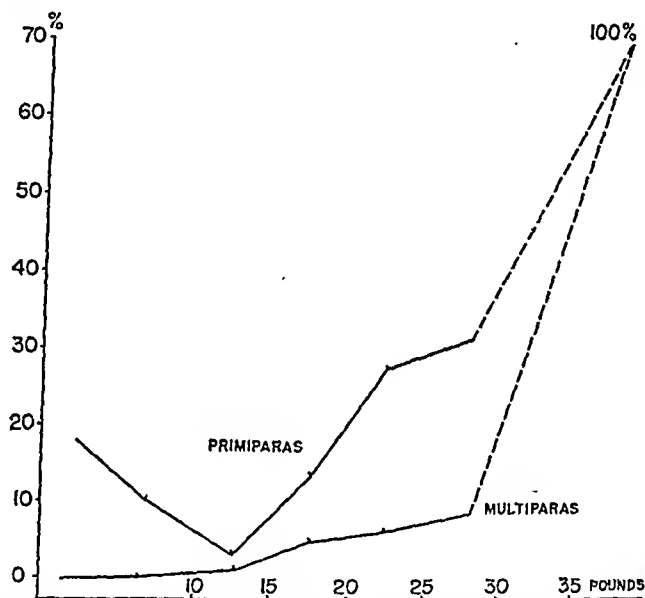


CHART 2. EFFECT OF WEIGHT GAIN, DIET AND FLUID BALANCE ON DYSTOCIA (LOUGHRAN)

The author is avowedly diffident about drawing conclusions from this small number of cases, but when he compares his findings with the standard, text-book figures for the duration of labor, he cannot help but wonder whether the regime described may not be responsible for this happy experience.

### SPINAL ANESTHESIA IN VAGINAL DELIVERY; A REPORT OF 1,547 CASES

R. T. WEAVER, D. L. ADAMSON AND F. L. JOHNSON

*Am. J. Obst. & Gynec.*, 51: 764-770, 1946

It is the authors' belief that there is a useful place in obstetrics for spinal anesthesia in delivery and that the dangers in its use have been greatly exaggerated.

Therefore, they present in this paper their results with small doses of spinal anesthesia during vaginal delivery in 1,547 patients, with reference to fetal and maternal mortality, difficulties, dangers and possible advantages. These patients were delivered during the 10-year period from Jan. 1, 1935 to Dec. 31, 1944.

There has been a notable increase in the number and percentage of patients delivered by this means at the authors' hospital. In 1935 only 2 patients (0.02 per cent of the total deliveries) had spinal anesthesia, whereas in 1944, of 3,410 deliveries, nearly 22 per cent received spinal anesthesia.

The technique is essentially the same as for intradural block. The anesthetic of choice is novocain crystals dissolved in about 2 cc. of spinal fluid, injected into the 3rd or 4th lumbar interspace without barbotage. The small dose employed, 50 mg., is sufficient to give a painless delivery, but does not materially decrease uterine contractions. The authors have found that difficulty in obtaining a satisfactory tap is an objection, more imaginary than real, to the use of spinal anesthesia.

In this series of 1547 patients receiving spinal anesthesia, there were 63 "failures", or 4.2 per cent. These include all patients receiving any other anesthetic whatever. There were 5 patients recorded as having some form of shock, but only one of these cases fits the commonly accepted picture of procaine hydrochloride shock. There were no maternal deaths in the entire series, either immediate or during the puerperium, from any cause. There were 43 stillborn babies and 17 neonatal deaths, giving a combined fetal mortality of 3.7 per cent. During the same period of time, the combined percentage in the authors' hospital was 5.1 per cent. During the past 5 years, when spinal anesthesia was used with increasing frequency, there was a progressive drop in stillbirths and neonatal deaths from 5.7 per cent in 1940 to 4.7 per cent in 1944.

In analyzing the 43 stillbirths, it was found that in only 8 patients was there a reasonable chance of obtaining a normal baby when the anesthesia was given. Of the 8, 2 were breech presentations in primiparas, one an internal podalic version after a long labor, one an abnormally large baby, one a 27-week premature, one had the cord twice around its neck and very tight, and 2 were midforceps deliveries. Of the 17 neonatal deaths, 11 had a considerable degree of prematurity, 3 had congenital abnormalities incompatible with life, one had hemorrhagic diathesis, one died of bronchopneumonia, and one from cerebral hemorrhage. Careful review of the hospital records fails to show the anesthetic drug as a contributing factor in any of these fatalities.

From experience with this series of patients, the following conclusions have been drawn:

- 1—Spinal anesthesia in small doses is a safe anesthetic for vaginal delivery.
- 2—Fetal loss is decreased. It is of special value in premature babies.
- 3—Analgesic drugs can be used with less danger.
- 4—Rapid pain relief is experienced in over 95 per cent of patients.
- 5—Obtaining an anesthetist is unnecessary.
- 6—Third stage and postpartum bleeding is diminished.

7—Nursing care is simplified.

8—Patients' satisfaction and approval are almost unanimous.

## THE INDUCTION OF LABOR WITH METHERGINE; PRELIMINARY REPORT

EMANUEL P. FARBER

*Am. J. Obst. & Gynec.*, 51: 859-865, 1946

The author reports the use of a new synthetic ergot preparation, methergine, for the induction of labor in 30 consecutive cases. Satisfactory results were obtained in 27 of these patients.

Routine induction of labor is not advocated, and only those patients in whom a specific indication for induction exists should be considered candidates for induction. The principle maternal indications are toxemia of pregnancy, pernicious vomiting, intrauterine fetal death and premature rupture of the membranes. Fetal indications are postmaturity and polyhydramnios. Maternal and fetal indications are premature separation of the placenta and placenta previa. Among the contraindications are any acute infectious disease, cardiac decompensation and cephalopelvic disproportion.

The preparation used in this study contained 0.25 mg. methergine per cc. All doses were given orally, diluted with about 10 to 15 cc. of water. In the first 11 cases only 5 minims of methergine were given every hour for 5 doses. In the remaining 19 cases the dose was increased to  $\frac{1}{2}$  cc. for the first dose and 1 cc. every 30 minutes thereafter for 4 doses. All of the cases conducted by the latter schedule were successful and no ill effects resulted from the increased dose.

Methergine was shown to have the ability to induce labor with intact as well as with ruptured membranes. There were no maternal or fetal complications. The length of labor was materially shortened in those cases induced with methergine and third-stage blood loss appeared to be less than in patients who went into labor spontaneously.

(Great caution must be exercised in using any ergot derivative for the induction of labor. I know of three cases in which ergonovine was given to pregnant women near term by mistake. All three patients had severe tetanic contractions and as a result, one of the babies died. Wolf has reported very unfavorable results from the use of ergonovine in the induction of labor. The dosage he employed was 0.25 mg. In a total of 10 cases, 3 with premature rupture of the membranes were successful. In 2 cases no pains ensued. In one case the patient had stormy but ineffectual pains for 10 hours and then the baby died; she went 8 days longer without pains and finally was induced successfully by other means. In 2 other cases uterine tetany set in after 6 to 23 minutes and lasted 2 to 3 hours; after this regular pains developed but when the babies were born 21 to 23 hours later, they both showed evidence of damage. (*Zentralbl. für Gynäk.*, 62: 1258, 1938.)

Methergine may possibly exert a different type of action than ergonovine, but as long as it is a derivative of ergot, some skepticism about its safety would seem to be in order.—Ed).

## AN EVALUATION OF THE HOGBEN PREGNANCY TEST

E. C. FOTTE AND G. E. S. JONES

Am. J. Obst. &amp; Gynec., 51: 672-677, 1946

The Hogben pregnancy test, based upon egg extrusion in the South African clawed toad (*Xenopus laevis*), has been found to be accurate between 96 and 100 per cent in some 5300 tests reported. Of these, no false positive result has as yet been recorded.

In the present paper the authors present the results of the Hogben test on 157 cases presenting diagnostic problems. These cases may be classified according to diagnosis as follows: 60 intrauterine pregnancies, 11 abortions, 2 ectopic pregnancies, one abdominal pregnancy and 68 nonpregnant cases.

There were 14 false negative results and 7 or 8 of these were performed before the 40th day of pregnancy. It would seem, therefore, that a normal intrauterine pregnancy cannot be diagnosed by the Hogben test with any accuracy before the 40th day of gestation. Following this period the expected accuracy approaches 96 per cent. Approximately two-thirds of threatened or incomplete abortions will give positive Hogben tests. Cases of corpus luteum cysts, suspected of being ectopic pregnancies, give negative reactions.

These results are comparable with those obtained with the Friedman test and show the Hogben test to be a satisfactory one for clinical use. The most important clinical advantage of the Hogben test is that it gives no false positive results.

## AN EVALUATION OF THE GUTERMAN PREGNANCY TEST

A. G. MORROW AND R. S. BENUA

Am. J. Obst. &amp; Gynec., 51: 685-691, 1946

Forty-nine specimens from 5 nonpregnant women were tested by the Guterman method. Nineteen positive and 2 doubtful tests were obtained. These results show that false positive tests for pregnancy are obtained frequently during the luteal phase in nonpregnant women. In one case of an apparently normal pregnancy of 7 weeks' duration, a negative Guterman test was obtained.

Guterman maintains that a positive test in the presence of amenorrhea indicates a normal pregnancy. There are several conditions in which this assumption is not valid; a positive test may be obtained when large amounts of 17-ketosteroids are present in the urine, as in arrhenoblastoma. In the presence of amenorrhea, the Guterman test may be positive on the basis of a functioning corpus luteum without pregnancy.

## HEMODYNAMIC CHANGES IN SALT DEPLETION AND IN DEHYDRATION

J. R. ELKINTON, T. S. DANOWSKI AND A. W. WINKLER

J. Clin. Investigation, 25: 120-129, 1946

The purpose of the present study is to correlate changes in the several compartments of the body fluid with the dynamic changes in the circulation following salt depletion and water depletion. Such a study should assist in defining the role of water and salt loss in the pathogenesis of traumatic shock.

Fasting unanesthetized female dogs were used for the experiments. Acute sodium chloride depletion was produced by the intraperitoneal injection of a specific amount of 5 per cent glucose followed by the withdrawal 4 or 5 hours later of an equal amount of peritoneal fluid containing salt. Acute water depletion in excess of salt was produced by the intravenous injection of a solution containing 10 per cent urea and 5 per cent glucose resulting in a copious diuresis. Total balances of water and chlorides were measured at the end of each experiment. Hemodynamic measurements were made before and after depletion in the following sequence: circulation time, cardiac output and arterial pressure. The effects of 4 or 5 hours of acute salt depletion were compared with those of 7 or 8 hours of acute water depletion. Thus, approximately equal degrees of contraction of extracellular fluid were produced in both groups of animals.

The results of these experiments showed that salt depletion in untraumatized animals produces a form of peripheral vascular collapse closely resembling that seen in traumatic shock. Plasma volume, cardiac output, circulation rate and blood pressure all decline sharply, and protein disappears from the plasma. Water depletion alone with a comparable decline in extracellular volume does not produce peripheral vascular collapse, although cardiac output, plasma volume, mean arterial pressure and circulation rate may decline. Usually very little or no protein disappears from the plasma.

The authors call attention to the loss of circulating protein with salt depletion. This loss of protein, so closely associated with the disproportionate decline in plasma volume, suggests a causal relationship. The implications of these experiments with regard to traumatic shock are clear. Extracellular salt depletion, if severe enough will cause shock without any element of trauma. In many forms of traumatic shock, such as that produced by temporary anoxemia of a limb, this factor of salt loss may outweigh all others in importance. In other types, such as that associated with hemorrhage, it may be less important. 4 figures.

## PATHOLOGY OF PREGNANCY

### PRECONCEPTIONAL PROGESTIN THERAPY IN HABITUAL ABORTION

ROBERT N. RUTHERFORD

Am. J. Obst. & Gynec., 51: 652-659, 1946

A brief report is presented investigating the use of progestin alone in the treatment of habitual abortion. The results are encouraging.

By definition, habitual abortion is limited to those cases who have had at least 3 sequential abortions and the patients included in this study were in this category. The husbands were of proved fertility and the patients were shown to ovulate regularly by endometrial biopsy if suspicion of abnormal catamenia was raised. Cervical erosion, adnexal or uterine tumors, malpositions of the uterus, all were corrected. Both partners were given a routine of balanced diet, adequate vitamin intake and accepted habits of rest and exercise.

Of a total of 63 cases, 54 had had 3 consecutive abortions and 9 had had 4 or more abortions. The patient was taught to calculate her fertile period as beginning some 18 days before flow was anticipated and continuing until the 10th day before flow. Exposure to pregnancy was made every other day during this period. The patient gave herself injections of 5 mg. of progestin every other day from the 18th day until flow supervened. If pregnancy occurred, the injections were continued every other day until the beginning of the 4th month, and then every 3rd day until fetal motion was felt.

Of the 54 patients having had 3 consecutive abortions, 31 went on to deliver viable infants although only 21 went to full term. Of the 10 who did not go to term, 3 infants died of prematurity. This would give a percentage of 57.4 delivered viable children, as compared with the expected fetal survival in this group of cases of 27 per cent.

Of the 23 cases who aborted, the incidence of proved pathologic ova was 69.1 per cent; the remainder were normal embryos with defective maintenance.

Of the 9 patients having had 4 or more consecutive abortions, only 4 cases carried to viability, with 3 full-term infants and one premature who survived. The salvage rate in this group was 44.4 per cent, as compared with an expected salvage of 6 per cent. Of the 5 patients in this group who aborted, 2 had normal embryos and 3 had pathologic ova.

This was a clinical study alone and no properly controlled hormonologic studies were carried out. The series of patients was small and is subject to further investigation. The author believes that there is no reason that this regimen should not be applied to any patient who has had a previous spontaneous abortion, whether progestin is used alone or with other agents.

## ACUTE RENAL FAILURE COMPLICATING ABORTION

J. V. O'SULLIVAN AND W. SPITZER

J. Obst. &amp; Gynaec. Brit. Emp., 53: 158-176, 1946

An extensive summary and analysis of the literature on renal failure complicating abortion has not been reported previously. Up to 1941 only 15 cases of abortion with renal failure among 48 cases occurring in pregnancy could be discovered. Since then, only 2 cases (Dingle's) and the authors' 2 have been reported. The poor prognosis is evident from the fact that up to the present time, only 9 cases of cortical necrosis in pregnancy with recovery can be found in the available literature.

In the present paper the authors present 6 cases of acute renal failure complicating abortion and one case of a multipara who developed acute renal failure following the injection of sterile glycerine into the cord for delayed separation of the placenta. A clinical and pathological study of these 7 cases shows that renal failure is one of the most serious complications of pregnancy. The ages of the patients ranged from 19 to 45 years; the majority of the patients fall in the higher age groups. There were 2 primiparae in the group, all of the remaining patients being multiparae. Thus, it would appear that multiparity predisposes to these renal complications. The 6 abortion cases were distributed from 12 weeks to 24 weeks of gestation. It is interesting that all cases of renal cortical necrosis occurred at a time when the placenta had already developed.

In regard to etiology, the authors group these renal complications into those which occur in non-septic abortions and septic abortions. It is emphasized that 5 out of these 6 cases of abortion were septic, a proportion which indicates the importance of infection as a factor in the causation of the acute renal insufficiency in this series. The possibility of the sulfonamides having some part in the etiology cannot, of course, be excluded.

The salient features of conservative treatment of oliguria and anuria following abortion are: (1) ample fluid intake to overcome the negative fluid balance; (2) alkaline fluids by mouth, prophylactically, for recipients of blood-transfusion; (3) high doses of ascorbic acid as a diuretic, and vitamin B<sub>1</sub> to prevent vomiting; and (4) maintenance of intake and output charts, and routine examinations of blood-urea and catheterized specimens of urine.

Decapsulation should have no place in the treatment of renal failure in these cases. Among the 9 recovered cases of renal cortical necrosis in pregnancy in the literature, 8 recovered without this surgical procedure. Both of the authors' patients upon whom decapsulation was performed died. Two of their cases with suppression of urine and azotemia responded excellently to bilateral splanchnic block with 1:2000 anethaine. 8 figures.

## ADVANCED ABDOMINAL PREGNANCY

P. COODIN

Canad. M. A. J., 54: 483-485, 1946

The following case is reported to illustrate some of the difficulties and complications of abdominal pregnancy.

The patient, a 29 year old primipara at full term, was admitted to the hospital for delivery on June 3, 1945. The expected date of confinement had been May 29, 1945, and since that day she had had backache and mid-abdominal pains at irregular intervals. The family history revealed that her mother's first pregnancy had been complicated by pernicious vomiting.

The patient's first admission to this hospital had been in November, 1944, when she was about 3 months pregnant. Her complaint at that time was constipation, nausea and vomiting and intermittent cramps in the upper abdomen. Her temperature on admission was 99.4, pulse 84, blood pressure 104/72. General physical examination was negative. Pelvic examination showed a softened cervix and lower uterine segment, and the uterine fundus reached the level of the pubic symphysis. Fallopian tubes and ovaries could not be palpated. A few days later she fainted, was seized with violent cramps in the lower abdomen and back, and vomited copious amounts of thick coffee-ground fluid. Temperature and pulse were elevated to 100.4 degrees F. and 120, respectively. Gradually her symptoms subsided and she carried on to full term with no untoward event. There was no vaginal bleeding at any time during pregnancy.

At the time of her second hospital admission physical examination was essentially negative. The fetal back and head could be palpated; the latter was engaged deep in the pelvis. No uterine contractions could be felt though the patient was visibly contorted with intermittent abdominal pains. An attempt to induce labor with castor oil, quinine and pituitrin was made on the day of admission and was repeated 2 days later without success. Several hours after the second induction the patient had epigastric pains and vomited clear fluid. By June 7, she appeared acutely ill, vomiting copious amounts of dark brown, foul smelling fluid. Her symptoms then resembled those at her previous hospital period in November. It was felt that she was suffering from some atypical form of toxemia and, because of her poor general condition, it was decided to empty the uterus by cesarean section.

Under spinal anesthesia the abdomen was opened and the peritoneum, omentum and fetal membranes were found glued together by adhesions. The fetus lay free in the abdominal cavity. Incision of the membranes resulted in profuse bleeding. The child was extracted and a considerable amount of old clotted blood was removed. The placenta was attached to the lateral and anterior abdominal walls, to the broad ligament, left ovary, several coils of small intestine and to the transverse colon. It was easily freed and removed. The left Fallopian tube was elongated and scarred. During removal of the placenta the patient

went into shock and hemorrhage became difficult to control. The incision was closed without drainage.

The newborn showed no gross abnormalities but died 21 hours after birth of atelectasis.

After operation the patient responded to blood transfusions, but a pinpoint perforation in the intestinal wall led to an accumulation of gas in the peritoneal cavity and necessitated incision for drainage 12 days postoperatively. The development of pneumonitis was treated by penicillin and the patient recovered. When seen one month after discharge, she was in excellent health.

Obviously, this patient had a tubal abortion during her first hospital period in November, 1944, as evidenced by the scarred Fallopian tube and old blood clots found at operation. However, the absence of vaginal bleeding and the predominance of vomiting caused the case to be mistaken for hyperemesis gravidarum on both hospital admissions.

## AN UNUSUALLY LARGE TUBAL PREGNANCY

ROBERT GREENE

West. J. Surg., 54: 247-249, 1946

The author presents the case of an exceptionally large tubal pregnancy. Although it was originally suspected that this patient had a tubal pregnancy, the suspicion was not confirmed until the mass had been removed from the abdomen. The patient, a 35 year old woman, was first seen on August 3, 1945, complaining of amenorrhea since June 5, 1945, with nausea, vomiting and severe cramping pain in the left lower quadrant, but no vaginal bleeding. Ectopic pregnancy was suspected, but the absence of bleeding and subsiding of pain suggested that she probably had a pregnancy of the left cornu of a bicornate uterus. As her course progressed, she had a normally enlarging tumor of the pelvis although she continued to have pain in the left lower quadrant. In October she began to have a brownish vaginal discharge, but never any bright bleeding. On December 20, fetal heart tones could not be elicited. An x-ray revealed the fetus in the mid-abdomen. Assuming that the fetus was dead, it was decided to wait for a spontaneous emptying of the uterus. On January 16, 1946, the patient exhibited symptoms of shock and intra-abdominal bleeding was suspected immediately. Because of an improvement in her condition and a rapid sedimentation rate, laparotomy was deferred until February 2, when the abdomen was opened and the left tube was removed intact. The uterus was very small and was so closely adherent to the enormous tube that the 2 masses had been palpated as one through the vagina.

The tumor measured approximately 20 cm. in its greatest diameter. The tissue was irregular in shape, lobulated and for the most part encapsulated. On

dissection, there were found the remains of a markedly distorted, somewhat macerated, partially absorbed fetus, measuring approximately 17 cm. in length. The pathologic diagnosis was "encapsulated fetus, placenta, blood clot from missed abortion of ectopic pregnancy of approximately 5 lunar months involving both fallopian and ovarian tissue." 1 figure.

## · CONCERNING TWO CASES OF FULL TERM ECTOPIC PREGNANCY

J. USEROS CASAS

Toko-Tinecologia Practica (Madrid, Spain), 5: 175-191, 1946

The author reports 2 cases of full-term ectopic pregnancy seen within a short period of 2 years.

*1st case:* A 43 year-old-woman, with menarche at the age of 18, and with 2 previous labors. The first one, prolonged, with dead fetus, followed by sepsis; the second one, normal, 17 years ago. L.M.P.: 2/15/42, normal. In the beginning of March, patient had metrorrhagia of 3 days' duration, which recurred again on March 15th, lasting until April 8. On April 26, she suddenly passed some blood, but had amenorrhea thereafter. On 11/12/42, examination revealed a fetus of 8½ months size, in longitudinal position, and it was interesting to notice that the feet could be felt as if they were just underneath the skin. The cervix was very high and, on the left side, a tumor like a child's head could be palpated giving the impression of being the uterus. Fetal auscultation was normal. However, due to the fact that it seemed so suggestive of the uterus, a diagnosis of full-term ectopic pregnancy or a pregnancy occurring in the cornu of a double uterus was made, and surgery advised in order to save the child's life. On laparotomy a uterus the size of a 3 months pregnancy was found with normal adnexa on the left. The right tube was very elongated and it circumscribed a cystic tumor the size of a full-term uterus laying entirely free within the peritoneal cavity. It was opened and a live fetus was removed, which however died one hour later in collapse. Due to difficulty in removing the sac, a subtotal hysterectomy was performed, followed by uneventful recovery. The placenta occupied more than  $\frac{3}{4}$  of the sac surface, and it was very flat.

This case seems to be a pure unruptured tubal pregnancy localized in the ampullar portion of the tube. This hypothesis is justified by the following facts: 1) Total freedom of the sac within the peritoneal cavity, with the exception of its inferior pole; 2) The external surface of the sac was shiny and smooth like peritoneum; 3) The disposition of the placenta, which occupied more than  $\frac{3}{4}$  of the cyst, was very flat and presented a velamentous insertion of the cord.

*2nd case:* A 32-year-old woman with 2 previous pregnancies, first labor normal and second one breech, both followed by normal puerperia. L.M.P.: 10/15/43. Following a period of two months of amenorrhea, the patient had some bleeding but without pain. At the third month, pains of contractile character developed

mainly in the left lower abdominal quadrant. After the sixth month the pains became more severe, especially with fetal movements. On 5/20/44, the patient was examined, when a 7 months old fetus was diagnosed in transverse position, with head lying on the left; a semi-solid tumor could be felt occupying the whole infra-umbilical region of the abdomen. The cervix was very high. Contiguous to it there was a transversely lobulated tumor, the inferior portion being of more solid consistency resembling an empty uterus, the size of a 3 month-old pregnancy. The other portion, softer, was adherent to the uterus.

On the basis of the history and pelvic findings, a diagnosis of ectopic pregnancy was made. On July 17, the patient stated that she had not been feeling fetal movements for the last 2 days, and also no pain. A laparotomy was performed some days later, which revealed a sac containing a small amount of liquid, and adherent to the bowel and omentum. It was in contact with the left uterine cornu at the level of the tube and round ligament insertions, which were free. The tube ran into the sac to a certain extent but finally exteriorised itself again, its fimbriated end being entirely free. The ovary was not included in the sac. The right tube also ran into the sac, inside which it could be followed. The sac was opened and a female, dead and macerated fetus was removed. A right salpingectomy and resection of left adnexa were performed together with removal of the sac, followed by uneventful recovery.

This case is evidently one of secondary abdominal pregnancy, belonging to the tubo-abdominal group. It seems that the pregnancy was formerly located in the isthmic portion of the left tube and, due to rupture of the latter, it became secondarily abdominal. Although the clinical data point toward a pregnancy occurring in the left tube, the pathological findings, on the other hand, indicate the right tube as the presumable site of the gestation (intrasacular position of the tube although it ended in a portion of the sac free of placenta). No pathologic changes could be detected in the tubes on microscopic examination.

(It would seem likely that both of these cases were instances of secondary abdominal pregnancy, in spite of the fact that the first was considered by the author to be full term pregnancy in an unruptured tube, and that the findings at operation were somewhat different from those seen with most secondary abdominal or broad ligament pregnancies. In the second case also, as the author states, the gestation was of the secondary abdominal type. Since the fetus had succumbed some time previously, the removal of the placenta was simple enough, which it is not when the fetus is still alive.—Ed.)

## HISTOGENESIS OF HYDATIDIFORM MOLE

NICHOLAS M. ALTER

*Am. J. Path.*, 22: 638-639, 1946

At the Margaret Hague Maternity Hospital 60 cases of true hydatidiform mole were observed in the last 15 years among 83,225 deliveries and 2,750 abortions, giving a proportion of one in 1,400 pregnancies.

Case 2 illustrates the clinical and pathological findings of a benign mole. Microscopically, villi were all without blood vessels. Over the surface anaplastic proliferation of trophoblasts was seen. The glycogen content in the benign type was marked. Mostly over the surface of Langhan's cells, syncytial giant cells were seen with vacuolated cytoplasm which often took fat stains. In the stroma regressive changes were seen with cyst formation; near the surface trophoblasts invaded the stroma and might be found at a distance.

The malignant course is typified by case 41. Malignant chorionepithelioma was found in the uterus removed 7 weeks after the mole. Upon microscopic examination a diffuse proliferation of small cuboidal cells was seen; there was no structural arrangement; necrosis and hemorrhage were extensive; the cells showed anaplasia, some mitotic figures, and pyknotic nuclei; they contained no glycogen.

Hydatidiform moles give a variety of histologic pictures depending on their situation in utero, regressive changes due to retention in utero, and changes after removal. Hydatidiform moles *in situ* naturally can give additional information. Such a uterine specimen was removed in case 7. On cross section a rather orderly arrangement was observed. Microscopic examination revealed more exuberant epithelial proliferation near the blood supply at the base than in the interior. Where trophoblasts were less proliferated and more differentiated they formed lacunae obviously for fluid exchange replacing vascularization; such channels could be observed over the surface as well as within the villi.

To extend this structural study, suitable specimens were pieced out from physiologic solution. One such preparation was 30 cm. in length. Microscopic sections of the alternating blebs and stems had epithelial covering of trophoblasts, which in places invaded the deeper layers and seemed flattened at the lining of the cavity. They formed also partly hyalinized masses within the stems. The blebs of the mole were analogous to retention cysts with retained material of metabolism due to complete lack of drainage. In material from abortions the avascular villi showed marked trophoblastic proliferation with bud-like outgrowth of branches.

The author summarizes by saying that a true hydatidiform mole is an epithelial neoplasm of the chorionic trophoblast with secondary cystic changes of the stroma in uniovular pregnancy. This epithelial proliferation shows various degrees of the histologic changes found in malignant growth: anaplasia and invasion, which are, however, intrinsic characteristics of these embryonal cells. Evidence seems to indicate that these proliferative changes are due to the disappearance of the allantoic circulation. Cystic changes of chorionic villi due to regression of the final vascular system are false moles, as observed in early abortion, ectopic and other uniovular pregnancies.

## CHORIONEPITHELIOMA

W. PELTON TEW

Canad. M. A. J., 54: 469-472, 1946

The author presents an historical review of this disease and a description of its pathology, clinical features and treatment. Four cases of chorionepithelioma are reported. Two of these are alive and well 7 years after operation and 2 have died. One of the 4 was associated with a hydatidiform mole. Three cases followed an early pregnancy or abortion and one followed a full or term labor.

Chorionepithelioma may occur in a typical or atypical form; both varieties seem to be equally malignant. In a few rare instances the primary growth may occur outside the uterus; several cases have originated in the Fallopian tube. Chorionepithelioma metastasizes rapidly. Dorland, in a presentation of 52 cases, reported metastasis to the lungs in about 75 per cent, to the vagina in 54 per cent, and to the brain in 5 per cent.

Chorionepithelioma may occur at any age during the childbearing period. It commonly follows a pregnancy, which may terminate in full term labor, abortion or hydatidiform mole. Hydatidiform mole is associated with the growth in about 50 per cent of cases. However, only about 5 per cent of the hydatidiform moles become chorionepitheliomas. The commonest early symptom is abnormal vaginal bleeding, and occasionally there are painful uterine contractions, nausea and vomiting. Early diagnosis is important, since early active treatment is the only treatment of any value. The final diagnosis is dependent upon 3 points: (1) history of continued bleeding after an abortion or labor; (2) the pathological findings from a diagnostic curettage; and (3) a positive Friedman test. This test is commonly strongly positive even in diluted specimens. The treatment of choice is a radical panhysterectomy for all cases where this is possible. This is followed by treatment with deep x-ray. When operation is not possible, a course of radium and deep x-ray is the only alternative, but this has yielded most unsatisfactory results in the author's experience.

The importance of a thorough investigation of any unusual bleeding following an abortion or even a full term labor is emphasized. An *early* diagnostic curettage and Friedman test are of paramount importance.

## TOXAEMIA OF PREGNANCY

SIMON GOLD

Canad. M. A. J., 54: 456-463, 1946

The classification of the toxemias of pregnancy recognized by the American Committee on Maternal Welfare is presented, and the author discusses the char-

acteristic symptoms of the condition. These include excessive gain in weight, usually associated with edema, hypertension, albuminuria and symptoms referable to the central nervous system. Symptoms of the renal, gastrointestinal and visual systems also appear.

The clinical importance and interpretation of generalized edema in pregnancy without hypertension and albuminuria are discussed. Sixty-five per cent of all pregnant women show some edema during pregnancy. In almost every normal case a diuresis begins about 24 hours after delivery and edema usually disappears within 5 days following delivery. Theories which have been postulated to explain pregnancy edema are briefly as follows:

1. Anselmino and Hoffmann and Levy-Solal suggested that excess posterior pituitary secretion was the responsible factor.
2. Poten thought that the enlarged uterus exerted pressure on the ureters.
3. Strauss, Barath and Weiner and Rona believed that increased hydrostatic pressure in the capillaries was responsible for edema.
4. Eastman and Strauss strongly supported the theory of hypoproteinuria.
5. Eufinger suggested the theory of plasma colloid instability.

The normal exchange of fluids between the blood stream and the tissues is a result of a fine balance between (a) the hydrostatic pressure of the blood in the capillaries which tends to force fluid out of the blood stream into the tissues and (b) the plasma colloid osmotic pressure which tends to draw fluid into the blood stream. If the colloid osmotic pressure of the serum proteins is less than 20 cm. of water, edema may occur. Such a low pressure usually is associated with a serum protein concentration of less than 5.5 gm.%. The average serum protein concentration in nonpregnant women is 7.5 gm.%, and in normal pregnant women, 6.5 gm.%. There is a decrease in serum protein concentration in pregnancy which occurs regardless of diet or protein intake, and which reaches a minimum at 30 weeks.

The author states that it is generally accepted that edema of pregnancy is not associated with increased hydrostatic pressure, capillary permeability to protein, anemia and vitamin B deficiency.

Dieckman and Wegner studied the serum proteins in relation to the increased plasma volume in pregnancy (up to 65 per cent above the normal nonpregnant level), and found that the protein was increased by 18 per cent at term above the normal nonpregnant level, but since the plasma volume was increased to a greater degree, there was an actual decrease in protein concentration. Thus, it would appear that the lowered protein was the result rather than the cause of water retention.

The retention of sodium parallels that of water. There is a positive balance of this ion during the latter months of pregnancy; part of this is attributed to the needs of the fetus, but there is also an altered capacity for excretion. Whenever edema forms, mineral salts, especially sodium, must be present. Administration of large amounts of sodium leads to water retention in normal individuals. The author concludes that the production of edema in pregnancy is a result of retention of the sodium ion.

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women served as controls. None of the women investigated in this study presented any history of previous cardiac disease.

The 2 women classified in Group 1 were 31 and 35 years of age, respectively. In both patients toxemia of pregnancy was manifested by hypertension, albuminuria and edema. Both patients experienced acute left ventricular failure during labor, but recovered with appropriate treatment. The electrocardiograms for these patients were characterized by the waxing and waning of the symmetrically inverted T wave in leads I,  $CF_2$  and  $CF_4$ , and of an upright symmetric T wave in lead III, the absence of any pronounced S-T deviation and the absence of changes in the QRS complex characteristic of myocardial infarction. These changes simulate those occasionally seen in acute nephritis.

It is of interest that neither patient complained of pain in the chest at any time nor did either patient show any lowering of the diastolic blood pressure at the time of cardiac failure. In one case no drop of the systolic pressure occurred.

In view of the pathologic observations in similar cases reported by others, the authors believe that the electrocardiographic changes were produced by focal myocardial necrosis, infiltration or edema rather than by a myocardial infarction secondary to occlusion of a coronary artery. The occurrence of coronary occlusion in a young woman without any history of antecedent cardiac disease would be most unusual. It would appear that the ultimate prognosis in patients who recover from cardiac failure in toxemia of pregnancy is better than that following coronary disease; therefore, a correct interpretation of the electrocardiographic pattern in these cases is of practical value. That the changes observed in the electrocardiograms of these patients with cardiac failure simulate those occasionally seen in acute nephritis is significant in view of the fact that the pathologic cardiac changes in acute nephritis, while different from those in toxemias of pregnancy, may also include edema with occasional inflammatory and degenerative changes of the cardiac muscle and its serous membranes.

The authors believe that the focal myocardial necrosis, edema and infiltration in toxemias of pregnancy are the essential factors which lead to a myocardial weakening and consequently may act as a precipitating mechanism in the cardiac failure.

Only 4 out of 10 cases of toxemia of pregnancy in which cardiac failure did not develop showed electrocardiographic abnormalities, and in none of these cases were the changes as pronounced as in the 2 cases which developed cardiac failure. In none of the 4 cases were patterns present resembling an atypical acute infarction of the anterior wall or acute nephritis.

Inversion of the T wave in leads  $CF_2$  and  $CF_4$  occurring during the last trimester of pregnancy and reverting to its normal upright form within one week following delivery is possibly a result of dilatation of the heart. This occurs in a small percentage of normal and toxemic patients.

Transient first degree auriculoventricular block may occur. One case is described in which this occurred in the postpartum period of a patient with toxemia of pregnancy. 6 figures.

The main features in the treatment of pre-eclampsia and eclampsia are bed rest, adequate sedation, and the production of water elimination by purges, restriction of salt and sodium in the diet and the use of hypertonic glucose solutions in water intravenously. In severe pre-eclampsia and eclampsia, intramuscular magnesium sulfate is indicated. The effect of parenteral magnesium on the nervous and cardiovascular systems is important; parenterally administered magnesium has an anesthetic effect, and is a powerful vasodilator and produces a decline in blood pressure.

Diet is of great value in the control of pre-eclampsia. Daily fluid intake is maintained at 2500 to 3000 cc. During the first 24 hours a milk and water diet is administered. Diet for the second 24 hours is the liquid or No. 1 toxic diet which is neutral ash and salt free. On the third day the patient is given the No. 2 toxic diet which is also neutral ash and salt free, and contains 100 gm. protein, 200 gm. carbohydrate, 80 gm. fat and has a total value of 2160 calories.

If the patient does not respond to treatment, as evidenced by a failure of diuresis or by maintained or rising blood pressure, evacuation of the uterus must be considered. If hypertension and albuminuria persist for 3 weeks, termination of pregnancy is imperative to prevent the development of permanent postpartum hypertension. The method by which the pregnancy is terminated depends on the type of pelvis and presence of disproportion, and the condition of the cervix. Most cases can be successfully managed by simple rupture of the membranes or bag induction. Cesarean section, with certain exceptions, should be avoided. The author presents 4 cases, 2 of pre-eclampsia and 2 of eclampsia.

Good prognostic signs in eclampsia are a diuresis and a drop in blood pressure that is maintained at or slightly above normal levels. The prognosis is poor if there is a progressive unexplained drop in blood pressure. 4 figures.

## ELECTROCARDIOGRAM IN TOXEMIAS OF PREGNANCY

L. WALLACE, L. N. KATZ, R. LANGENDORF AND H. BUXBAUM

Arch. Int. Med., 77: 405-419, 1946

An examination of the electrocardiographic records of 12 patients suffering from toxemia of pregnancy without eclampsia revealed that they fell into 3 groups. Group 1 consisted of 2 cases in which the electrocardiographic patterns suggested an acute myocardial infarction of the anterior wall. Both of these cases presented a classic picture of toxemia of pregnancy and resulted in acute left ventricular failure at the time of labor. Group 2 was made up of 4 cases which did not result in cardiac failure but in which, nevertheless, changes were manifested in the electrocardiogram. Group 3 consisted of 6 cases in which there was no evidence of cardiac failure and in which no electrocardiographic abnormalities were seen despite the presence of toxemia. Electrocardiograms for 5 normal pregnant

## ANTIDIURETIC ACTIVITY IN THE BLOOD OF NON-PREGNANT WOMEN AND WOMEN DURING NORMAL AND TOXEMIC PREGNANCY

VERA I. KRIEGER AND T. B. KILVINGTON

J. Clin. Endocrinol., 6: 320-324, 1946

A review of the work which has been published on the relation of the anti-diuretic hormone secreted by the posterior lobe of the pituitary gland to the causation of eclampsia reveals much controversy of opinion. Anselmino, et. al., claimed to have detected antidiuretic hormone in the blood of patients suffering from eclampsia and severe toxic albuminuria of pregnancy. Other workers failed to detect the hormone in the blood of patients with pre-eclampsia and severe toxemia of pregnancy. Theobald supports Anselmino's claim by finding antidiuretic substance in the ultra-filtrates from the blood of 2 eclamptic patients. Other workers have found antidiuretic substance in the blood from males and non-pregnant women, and in the blood of patients with hypertension of various kinds.

In 1940 the authors published results of a study of urine from non-pregnant women, from pregnant women and from women suffering from toxic albuminuria and eclampsia. The results showed that small amounts of diuretic substance were present in the urine of some non-pregnant women, more often in that of normal pregnant women, and frequently and in much greater concentration in the urine of women with pre-eclampsia and eclampsia. Throughout the investigation 100 cc. samples of urine from the patients being tested were assayed. Area differences were obtained by plotting time against the total volume of urine excreted in 5 hours by groups of 4 male rats; the units of abscissa and ordinate were 60 minutes per inch and 10 cc. per inch, respectively. The ranges of values for the different groups were as follows: non-pregnant women, 0.16-1.73 sq. in.; normal pregnant women, 1.83-3.45 sq. in.; toxemic women, 1.93-5.45 sq. in.; eclamptic women, 5.17-8.70 sq. in.

Since the publication of the work described above, the authors have found that an area difference of 5.6 sq. in. is the minimum value representing a true anti-diuretic effect. Consequently, their previous conclusions must be modified, and they believe now that true antidiuretic effects were obtained only in the group of eclamptic women mentioned above.

In a recent study the authors examined blood from 303 women, including non-pregnant women, women during normal pregnancy and women with eclampsia. In the normally pregnant the tests were made (a) during the early months, (b) between the  $7\frac{1}{2}$  and  $8\frac{1}{2}$  months of pregnancy, (c) at term and (d) during the puerperium. While there was evidence of some antidiuretic activity in the blood of 20 per cent of the non-pregnant women, no activity was found in the blood of any patients examined during early pregnancy and in only 8 per cent of those tested between the 30th and 38th weeks of pregnancy. However, anti-

(If we may judge from the several series of autopsies which have been reported in fatal cases of eclampsia, degenerative changes in the heart muscle are frequent accompaniments of that disease. The most commonly quoted papers perhaps are the two early studies of the German pathologist, Georg Schmorr (Pathologisch-Anatomische Untersuchung über Puerperal Ekalmpsie, Vogel, Leipzig, 1893; and Arch. für Gynakologie, 65: 517, 1902). Disregarding cloudy swelling and fatty degeneration, which were very frequently present, he found hemorrhage and necrosis in the myocardium in 43 of 73 autopsies. "In the neighborhood of the hemorrhages the muscle fibers were disintegrated into hyaline layers, usually with the nucleus gone and the transverse striations no longer recognizable." In more modern times, Polak, and Polak and Beres have demonstrated degenerative changes in the heart in 94 of 102 post-mortem examinations (J. A. M. A., 87: 226, 1926; and Am. Jour. Surg., 4: 143, 1928).

Clinically, the frequency of pulmonary edema and cyanosis in severe eclampsia surely suggest heart failure. Indeed, they impressed Stroganoff so strongly in this way that he included digitalis in his regime of therapy a few years ago. Paul White, in his well known book "Heart Disease", writes: "Associated with acute hypertension in the toxemias of pregnancy (eclampsia) there may be serious toxic myocardial dilatation with acute heart failure and pulmonary edema."

The above article by Wallace, Katz, Langendorf and Buxbaum comes, of course, from one of the leading electrocardiographic laboratories in the country and when its weight is superimposed on the evidence above cited, it would seem forever settled that cardiac alterations are rather common accompaniments of pre-eclampsia and eclampsia.

This, however, is by no means the case.

On the other side of the question, Burton E. Hamilton, perhaps our leading authority on heart disease in pregnancy, takes a very strong stand, stating: "Our present opinion is that uncomplicated pre-eclampsia or eclampsia cause neither heart failure nor significant acute myocarditis". Over the years he has apparently carried out a searching study of this problem and is still looking for a case where undoubted myocarditis of clinical importance appears during uncomplicated eclampsia or pre-eclampsia. In his occasional consultations on patients with definite or suspected pre-eclampsia and in a few with eclampsia, he had taken electrocardiograms and has not found convincing evidence of acute myocarditis in a single case. Seven patients were seen by Hamilton at the Boston Lying-In Hospital who had severe pre-eclampsia and complained of epigastric pain. Electrocardiograms were taken for the purpose of obtaining evidence to associate this pain with the heart. He interpreted the electrocardiograms as negative. In regard to edema of the lungs, he finds from discussions with various pathologists that there is little or no evidence in these cases of venous congestion in the lungs and liver, whereas in patients dying with congestive heart failure, evidences of venous congestion in the lungs and liver are always abundant. He reports, moreover, a general agreement among the pathologists to whom he has talked that no special evidence of severe acute myocarditis has yet to be discovered in uncomplicated pre-eclampsia or eclampsia. (Hamilton and Thomson: The Heart in Pregnancy and the Childbearing Age, Little, Brown & Co., Boston, 1941).

We have here then a striking difference of opinion between two of the leading cardiologists of the country about the heart in pre-eclampsia and eclampsia. This is a most important practical problem for it has to do with such questions as the justification of digitalizing pre-eclamptic and eclamptic patients. In view of this controversy, it might be a good idea if obstetricians would request electrocardiograms on their severe cases of pre-eclampsia and eclampsia, have them read by a competent cardiologist and, after a reasonable number has been accumulated, report them.—Ed.)

The results of the present study are presented in Table II. Of these 5 diabetic women, 3 who had had no signs of toxemia of pregnancy had normal levels of pregnanediol throughout the periods studied. One patient, with mild toxemia, had a low excretion of pregnanediol for several weeks. The patient with severe toxemia showed a relatively low excretion at the time of onset of toxic symptoms. It is interesting to note that pregnanediol excretion did not fall after intrauterine death in one patient whose levels were normal before fetal death occurred.

Neither toxemia nor fetal mishap was found to be associated with any decreased excretion of estrone-estradiol, but a decreased excretion of estriol was found to be associated with both cases of toxemia, and with one of 2 cases of fetal mishap without toxemia.

In 2 of 3 patients who had no signs of toxemia the serum gonadotrophin levels were normal, and in the third patient the levels were significantly increased. Of 2 patients with clinical signs of toxemia, one patient with mild toxemia had

TABLE II

*Results of studies of urinary pregnanediol and estrogen excretion and serum chorionic gonadotrophin in five diabetic pregnancies*

PATIENT	CLINICAL CONDITION	FETAL DEATH	HIGH CHORIONIC GONADOTROPHIN	LOW ESTRIOL	LOW ESTRONE-ESTRADIOL	LOW PREGNANEDIOL
Mrs. M.....	Normal	0	0	0	0	0
Mrs. DaL.....	Normal	+	0	+	0	0
Mrs. K.....	Normal	+	+	0	0	0
Mrs. L.....	Toxemic	0	0	+	0	+
Mrs. T.....	Toxemic	0	+	+	0	+(?)

normal levels of chorionic gonadotrophin, and the other patient with severe toxemia had significantly increased levels of gonadotrophin. Fetal mishap was associated with both normal and high levels of gonadotrophin.

The authors conclude that neither low estriol nor low pregnanediol excretion is consistently associated with fetal death, but that a lowered excretion of both appears to be associated with toxemia. Both fetal death and toxemia may or may not be associated with increased serum chorionic gonadotrophin. Hormone abnormalities were demonstrated in both patients with fetal mishap, but in one case the abnormality consisted of an increased serum level of chorionic gonadotrophin and in the other case of a decreased excretion of estriol. White's theory that fetal death is associated with toxemia was not borne out by this small series.

The authors' finding of high serum chorionic gonadotrophin levels in a patient with normal estriol and normal pregnanediol excretion is not in keeping with the theory that the increased output of chorionic gonadotrophin is an attempt to compensate for a lack of estrogen and progesterone. Further evidence against a close reciprocal relationship between the amounts of these 2 hormones is seen in the fact that pregnanediol excretion was unchanged following fetal death, while the serum gonadotrophin levels were strikingly lowered.

diuretic activity was present in the blood of 41 per cent of the patients at term and in 37 per cent of those tested 3 to 8 days post partum. The blood of 29 per cent of the women with eclampsia showed antidiuretic properties.

These results suggest that the occurrence of antidiuretic substance in the blood may be a normal physiological process associated with labor and the puerperium. They do not support the claim that antidiuretic hormone is a factor in the causation of eclampsia.

## HORMONE METABOLITES IN BLOOD AND URINE OF DIABETIC PREGNANT PATIENTS WITH AND WITHOUT TOXEMIA

BETTY L. RUBIN, R. I. DORFMAN AND M. MILLER

J. Clin. Endocrinol., 6: 347-368, 1946

The present study consists of an evaluation of the serum and urine chorionic gonadotrophin and of estrogen and pregnanediol excretion in 5 pregnant diabetic women throughout the latter part of pregnancy. Of these 5 women, 2 developed toxemic symptoms but were delivered of normal babies, while 3 had asymptomatic pregnancies with respect to toxemia, but one of the latter group was delivered of a macerated fetus, and the infant of another died within a few hours of birth.

A review of previous investigations on the hormone metabolite concentrations in the urine and blood of toxemic patients leads to the conclusion that toxemia of pregnancy is often associated with an abnormal metabolite pattern. Various workers have noted an increase in serum and urine levels of chorionic gonadotrophin and a decrease in serum and urine levels of estrogen. Also, a lowered excretion of pregnanediol has been observed in association with toxemic pregnancy.

In normal pregnancy there is an increased excretion of pregnanediol as pregnancy progresses, from 17-30 mg. per day at week 20 to a peak of excretion between weeks 32 and 35 with a range of values from 30-130 mg. per day. Within 24 hours of delivery the compound has practically disappeared from the urine. There is also an increase in urine estrogen values in the progression of normal pregnancy, with values from 10-15 mg. per day during the seventh and eighth months and a rise to 15-40 mg. per day in the ninth month. The curves for estriol, estrone and estradiol are similar. As with pregnanediol, the hormone rapidly disappears from the urine following delivery. Serum chorionic gonadotrophin in normal pregnancy maintains a fairly constant level, up to 3000 I.U., throughout the latter part of pregnancy, although a slight rise, as high as 5000 I.U. in the last month and 7500 I.U. just before term, is not abnormal. Urinary gonadotrophin excretion is also fairly constant, between 7000 and 30,000 I.U., with a possible rise to 50,000 I.U. just before term. This hormone also disappears rapidly from the serum and urine immediately following delivery.

Short period uric acid and urea clearances had become normal in the majority of cases in the early puerperium. Those cases in which the short period clearances were not normal were the same as those few which exhibited abnormal 24-hour uric acid clearances.

The authors conclude that there may be a hyperuricemia or a hyperuremia, or both, in eclampsia and severe pre-eclampsia, and that these elevations may be due largely to an altered kidney function. A decrease in the glomerular filtration rate may serve to explain the phenomena in the majority of cases. However, some of the exceptional cases can be explained only by postulating a change in the rate of tubular reabsorption of uric acid and urea. The possibility also exists that some of these changes may be due to alterations in the metabolism of these substances.

#### ON THE INCREASED URIC ACID CLEARANCE FOLLOWING THE INTRAVENOUS INFUSION OF HYPERTONIC GLUCOSE SOLUTIONS

R. W. BONSNES AND ETHEL S. DANA

*J. Clin. Investigation*, 25: 386-388, 1946

Previously the authors had observed that the uric acid clearance was not altered by the injection of 50 ml. of 50 per cent glucose, concluding, therefore, that the active and maximal reabsorption of glucose had no effect upon the simultaneous reabsorption of uric acid. However, Talbot has reported an increase in uric acid excretion when the blood glucose is maintained at relatively high levels (400 mgm. per cent) by continuous glucose infusion. In view of this apparent contradiction the authors have determined the uric acid and urea clearances during the continuous infusion of glucose, and the results obtained confirm the correctness, at least in part, of both reports.

The rate of uric acid excretion and therefore the uric acid clearance is markedly increased when the blood glucose is maintained well above normal physiological levels. The rate of uric acid excretion seems to be a function of the increase in the blood sugar level. With the blood sugar maintained at an average value of 499 mgm. per cent, the average uric acid clearance increased in 4 patients 2.57 times the control clearances. At the same time the urea clearance and the rate of creatinine excretion increased only 1.25 times the values observed during the control periods.

These experiments show why the authors did not observe any changes in the uric acid excretion in their previous work (mentioned at the beginning of this abstract). In those experiments glucose was given in a single 50 ml. injection of 50 per cent glucose and the urines were collected in 3 separate one-hour periods following the injection. The blood sugar levels should have been high for 15 to

It may be noted that the only patient in this series to show normal hormone levels throughout pregnancy was the only patient to have a normal pregnancy with respect to toxemia and to fetal mishap. 6 figures.

## A SURVEY OF THE TWENTY-FOUR-HOUR URIC ACID AND UREA CLEARANCES IN ECLAMPSIA AND SEVERE PREECLAMPSIA

R. W. BONSNES AND H. J. STANDER

J. Clin. Investigation, 25: 378-385, 1946

Recently it has been shown that the uric acid clearance in eclampsia and in severe pre-eclampsia is decreased, and earlier work showed the urea clearance in this disease to be decreased. More recent studies have shown a decreased glomerular filtration rate as the outstanding alteration in kidney function in the late toxemias of pregnancy. Therefore, one might expect a general increase in the level of several blood constituents in the late toxemias of pregnancy as a result of this decreased glomerular filtration rate. In view of these observations, the authors have studied further the uric acid and urea clearance in the late toxemias of pregnancy in order to determine if there were some cases which are classified clinically as eclampsia or severe pre-eclampsia which might have a normal kidney function with respect to one metabolite, such as urea, and an abnormal function with respect to another metabolite, such as uric acid.

Twenty-four urines were collected from 32 cases of late toxemia of pregnancy (3 cases of antepartum eclampsia, 2 cases of questionable postpartum eclampsia and 27 cases of severe pre-eclampsia). Only the uric acid clearances were determined on 7 cases, and both uric acid and urea clearances were obtained on the remaining 25. In spite of certain potential sources of error in these studies, the 24 hour clearances do yield information which may be obtained practically, as to the average 24-hour performance of the kidney and as to the relative rate of change in this function.

The uric acid and urea clearances were found to be subnormal during the active phase of the disease and to return to nearly normal values by the third to fourth postpartum day in the majority of cases (15 out of 23). However, certain exceptions to this general behavior were found. Four patients showed subnormal uric acid clearances during the disease, which improved during the early puerperium as above. But the urea clearances remained normal throughout the period that these patients were under observation. Two patients showed apparently normal uric acid clearances and urea clearances during the antepartum period, but decreasing urea with normal uric acid clearances during the early puerperium. Finally, 2 other patients had subnormal uric acid clearances during both the antepartum and the early puerperium. In one of these cases the urea clearance was a low normal, while in another it was definitely subnormal.

4 patients who responded to orally administered crude liver extract differs from that in the 2 patients who responded to large amounts of more refined liver extract.

Since a distinction in therapeutic response to refined and crude liver extracts was first reported in anemic monkeys, and later in patients by Dr. Lucy Wills and her associates, the authors suggest that this effective principle in crude liver extracts and in autolyzed yeast be designated as "Wills' factor." It clearly differs from the principle in liver which is effective in Addisonian pernicious anemia and from the so-called extrinsic (food) factor.

Observations on one of the 4 cases indicated that Wills' factor is not identical with various pure components of the vitamin B complex and accessory nutritional substances, including biotin, *L. casei* factor and pyridoxal.

In instances of macrocytic anemia refractory to parenterally administered liver extract, especially those associated with pregnancy, it may be of practical therapeutic importance to test the efficacy of relatively crude liver extracts administered orally or, when suitably prepared, administered intravenously in large amounts.

The demonstrated therapeutic value of orally administered liver extracts in occasional patients with nutritional macrocytic anemia due to a deficiency of Wills' factor should not obscure the well-established advantages of parenterally administered refined liver abstracts in the treatment of the majority of patients with nutritional macrocytic anemias, especially those with Addisonian pernicious anemia. 5 figures.

## EMOTIONAL FACTORS IN THE COURSE OF PREGNANCY

RAYMOND SQUIER AND FLANDERS DUNBAR

Psychosom. Med., 8:161-175, 1946

The objective of this paper is not to prove anything, nor is the paper a statistical one. Rather, it includes the description of 2 cases with the purpose of presenting some facts which may be of value in understanding the psychosomatic aspects of pregnancy, abortion and the puerperium.

Both of the patients whose case reports are presented were of superior intelligence; both scorned their mothers and identified themselves with their fathers; both were frustrated in their careers; both were frigid (although both recovered after adjustment to parenthood); and both were concerned about the sex of the baby. These 4 factors have been found in a number of other patients who present the pattern of abortion, premature delivery or stillbirth. One of these 2 patients, after a series of abortions and stillbirths, produced a living child in the eighth month of her fifth pregnancy. During this pregnancy she was under the care of a psychiatric consultant. The second patient whose case is described in this paper delivered a full-term infant as a result of her first pregnancy. The child was pallid and apneic and all measures of resuscitation failed to save its

30 minutes following glucose administration, and the tubular excretory mass for glucose would have been exceeded only during this time. However, the authors' earlier conclusions were correct in part, since glucose in the kidney tubule at physiological levels does not affect the uric acid reabsorption. Decrease in the rate of uric acid reabsorption occurs only when the glucose in the kidney tubule is maintained at levels in excess of the ability of the tubule to reabsorb the glucose.

These results also confirm Talbot's results qualitatively but not quantitatively. This quantitative difference may be due to a difference in the specificity of the methods used for determination of uric acid.

Some of the factors which may be operating to produce these results are discussed.

### NUTRITIONAL MACROCYTIC ANEMIA, ESPECIALLY IN PREGNANCY; RESPONSE TO A SUBSTANCE IN LIVER OTHER THAN THAT EFFECTIVE IN PERNICIOUS ANEMIA

JANET WATSON AND W. B. CASTLE

Am. J. M. Sc., 211: 513-530, 1946

The authors have studied 3 cases of nutritional macrocytic anemia, 2 of which occurred during pregnancy; these patients were shown under controlled clinical conditions to respond to orally administered liver extract immediately after failing to respond to multiple U.S.P. units (injectable) of parenterally administered liver extract. A fourth case responded immediately to parenterally administered liver extract when the dose was increased tenfold. Since this indicated response to a substance other than the hematopoietic factor presumably common to all liver extracts effective in Addisonian pernicious anemia, it seemed desirable to present these cases and to review apparently similar cases in the literature.

As a result of a review of the literature, as well as of the observations on these 4 cases, it is apparent that at least 2, and possibly 3, types of nutritional deficiency are involved in nutritional macrocytic anemias, as evidenced by differences in therapeutic responses to various types of liver extracts. These may be stated briefly as follows:

- 1—Response to usual amounts of the most refined liver extracts administered parenterally. This is a large group, including Addisonian pernicious anemia and many cases of sprue and macrocytic anemia of pregnancy.
- 2—Response *only* to orally administered crude liver extracts or to large amounts of certain relatively crude liver extracts given parenterally. This group includes certain instances of macrocytic anemia of the tropics, of anemia of pregnancy and of "refractory" anemias with megaloblastic bone marrow, as well as the cases presented in this paper.
- 3—As to a third type, it is possible that the basic deficiency in 2 of the authors'

gravidarum, who obtained little or no relief following a wide variety of symptomatic treatments, were completely relieved of their subjective symptoms following the use of hypnosis. Hypnosis was employed either with direct suggestion or with hypno-analysis and age regression. All patients except 2 were completely relieved utilizing these methods.

Four cases are presented which are typical of the authors' methods and results. The psychogenic factors responsible for the vomiting are revealed.

This form of therapy may act either by raising the vomiting threshold directly or by preventing contractions from the gastrointestinal tract reaching the higher sensorium. Again, the method of eliciting latent psychogenic factors responsible for the nausea and vomiting and bringing these to the surface and integrating them into consciousness is also a convenient, time-saving and most effective therapeutic procedure for permanently relieving this ordinarily refractory condition.

The authors believe that this valuable adjunct in the treatment of nausea and vomiting of pregnancy should be utilized by obstetricians.

## GESTATIONAL NEURONITIS

A. M. AGNEW

Am. J. Obst. & Gynec., 51: 758-763, 1946

Gestational neuronitis was first noted in the literature in 1854 and for many years hysteria was considered the etiological factor. In about 1887 the theory of autointoxication was suggested and, until the present time, was the generally accepted theory of causation in this country. In 1930, however, Theobald suggested that the neuritis of pregnancy was due to a vitamin B deficiency, the symptoms of beriberi being indistinguishable from those of polyneuritis of pregnancy. Since then, clinical and laboratory investigations have tended to strengthen the theory of a deficiency disease, and it is suggested that the problem may possibly bear some relationship to other toxemias of pregnancy.

In discussing symptomatology and clinical course of gestational neuronitis, the author divides this disease into 3 types: mild, severe and fulminating. In the *mild* group of cases the symptoms are: persistent tingling, or pain, or sensations of numbness in feet or hands, and neuritic pains in the arms and legs. These symptoms usually appear in the 4th month or later in a patient who has had a troublesome degree of nausea and vomiting in the early weeks, and are not progressive in character. Usually, after a varying length of time, they regress or disappear.

In the *severe* type, the almost invariable history is a moderately severe form of nausea and vomiting which has responded well to hospital treatment. After a short time, the vomiting recurs and the patient complains of tingling pains in the feet and severe neuritic pains in the legs. There is also a weakness which inter-

life. The cause of death was not determined satisfactorily by the obstetrician. Her second pregnancy resulted in a normal child which survived. During delivery, her psychiatric consultant was present and obviously facilitated the patient's progress.

Both of these patients had bleeding and gastrointestinal symptoms, including nausea, vomiting and colitis, during earlier pregnancies, but these symptoms were notably absent in a later pregnancy during psychosomatic treatment.

Whatever may be the internal or external agents predisposing to abortion, it appears from these histories and from other unpublished material that some persons develop an abortion habit just as others develop an accident habit, and that this habit may be interrupted by well-directed psychosomatic treatment.

The province of the consultant in psychosomatic medicine is unfortunately very foreign to most obstetricians. The consultant examines large areas of the patient's emotional and physical functioning which, if even suspected by the obstetrician, have been left untouched and unexplored. A knowledge of these areas (which are related to conception, pregnancy and delivery) may be instructive and prevent mistakes in the handling of a case. Although what may be called "psychosomatic obstetrics" is only beginning to take form, there is promise of its great utility in the future.

The obstetrician should weigh what he says to his patient. His verbal contact, like that of his mechanical and sterile technique, should not be neglected lest it traumatize her.

From this study there are suggestions that some of the clinical phenomena (such as nausea and vomiting, and some instances of bleeding) which puzzle obstetricians can be elucidated by the application of psychosomatic medicine.

In addition to the material presented in this paper, the authors discuss the relationship of psychic factors in the mother with the neonatal development of the infant. The pediatrician, the consultant in psychosomatic medicine and the obstetrician in one particular case, all have reason to believe that the mother's solution of her own emotional problems was largely responsible for a change in the health and behavior of her child. It is suggested that a psychosomatically sensitive obstetrician might pass on to the pediatrician who is similarly sensitive, certain personality data that can be utilized by the pediatrician in his care of the infant in cooperation with the mother.

## THE PSYCHOSOMATIC TREATMENT OF HYPEREMESIS GRAVIDARUM BY HYPNOSIS

W. S. KROGER AND S. T. DeLEE

Am. J. Obst. & Gynec., 51: 544-552, 1946

Nineteen cases of nausea and vomiting of pregnancy of varying intensity, ranging from the exaggeration of physiologic vomiting to true hyperemesis

by comparing the patients who had myomas over 6 cm. in diameter to patients who had myomas that were less than 6 cm. in diameter. Myomas of 6 cm. or more in diameter have been considered as large or significant because of the relationship of myomas of this size to dystocia. In this series, no myoma less than 6 cm. caused any difficulty during delivery, and in the majority of cases where obstruction occurred the myomas were larger. Thirteen patients had definite dystocia due to myoma.

Since myoma uteri are more frequently found in the late childbearing ages, there was a high incidence of elderly primigravidas (15.7 per cent). In direct relationship to this older age group, there was an increased incidence of toxemia.

The significance of myoma uteri in causing sterility is difficult to evaluate. It is during the first half of the childbearing period that a woman is most apt to become pregnant, but later the development of fibroids becomes more pronounced.

Unfortunately, in many cases, myoma uteri is overlooked during the course of pregnancy. Myomas are more readily detected in early pregnancy or post partum when the entire surface of the uterus can be explored on bimanual examination. Frequently they are discovered only when complications of pregnancy and delivery focus attention on them.

Pain is a symptom which is often associated with myomas in the rapidly growing pregnant uterus. Antepartum pain due to myoma was present in 11 per cent of the patients in this series. However, no myomectomies were performed during pregnancy because of pain, as recent studies have shown that myomectomy during pregnancy carries a high fetal mortality and an increased maternal risk.

The incidence of abortion (17.1 per cent) and of premature labor (5 per cent) in this series was twice the clinic incidence, which is 8 per cent and 2.5 per cent, respectively.

In those pregnancies progressing to viability, there was a notable increase in abnormal presentation. Of 298 pregnancies, vertex presentation occurred in only 90.6 per cent. Presentation is affected only by large tumors which interfere with the adaptation of the fetus to the longitudinal axis of the uterus.

There was no evidence that myoma uteri is a factor in causing prolonged labor or premature rupture of the membranes. Prolonged labor was observed in 9.1 per cent of the entire series, and the corresponding figure for the general clinic is 9.1 per cent. Premature rupture of the membranes occurred in 17.3 per cent of the entire series, while the incidence for the general clinic is 36.1 per cent.

There was a high incidence of operative delivery among the patients with large myomas (47 per cent) compared with patients with small fibroids (23.4 per cent) who have an incidence similar to the general clinic.

Postpartum hemorrhage is rarely caused by myomas. The incidence of postpartum hemorrhage among these patients was 3.8 per cent, an incidence similar to that found in the general clinic, which varied from 1.7 per cent to 4.4 per cent during the same period of time.

The incidence of puerperal sepsis was 15.8 per cent, or over twice as high as

feres with standing and walking, and often there are periods of forgetfulness and mental confusion. Examination shows general weight loss, marked atrophy of the muscles and diminished ankle and knee jerks. The vomiting usually persists with a steady progression of symptoms. Complete paralysis, with loss of the reflexes, starts in the toes and feet and gradually extends upward, involving the legs, bladder and rectum, abdominal muscles and diaphragm. There is often a dimming of vision progressing to a complete loss of sight. Chest and heart are negative, except for a persistent tachycardia, and the blood pressure remains normal. Urine, blood chemistry and spinal fluid show no changes. The paralysis progresses and death occurs with respiratory failure.

In the *fulminating* type, the symptomatology is the same as in the *severe* type, but the development and progress of the disease are much more acute and rapid; death may occur in 2 to 4 days from the onset of symptoms.

This disease should be considered a serious complication of pregnancy. McGoogan, in a review of 145 cases, found that there were 40 deaths, a mortality rate of 27.5 per cent. In 105 of these patients who received no vitamin B therapy there were 37 deaths (35.2 per cent) and in the remaining 40 patients who received varying amounts of vitamin B, there were 3 deaths (7.3 per cent).

Recovery, though slow, is usually complete. The cardiovascular and visual symptoms disappear quickly, the neurological symptoms over a period of from 3 to 18 months. A few cases with resulting permanent paralysis have been reported.

Treatment should consist chiefly of prevention with large doses of vitamin B as treatment for the nausea and vomiting of early pregnancy, together with iron and liver and a high vitamin diet for the remainder of pregnancy. In the treatment of the severe type, it would seem that either much higher dosages of vitamin B are needed, or that the prolonged vitamin deficiency has resulted in the establishment of some irreversible process which ends only with the termination of pregnancy.

The author presents 2 case reports; in each of these a cure was effected by therapeutic abortion.

## THE SIGNIFICANCE OF MYOMA UTERI IN PREGNANCY

FLORENCE A. DUCKING

Am. J. Obst. & Gynec., 51: 819-831, 1946

This study includes all of the cases of pregnancy complicated by myoma uteri at the author's clinic during the 7-year period between Jan. 1, 1937 and Dec. 31, 1943. There were 361 cases of myoma uteri in 22,283 pregnancies, an incidence of 1.4 per cent. If abortions are excluded, the incidence is lowered to 1.3 per cent.

The author evaluates the complications caused by myomas during pregnancy

Most cases should be treated promptly by surgery, but traumatic cases in young individuals with healthy musculature of the rectus muscle and a small hematoma do very well with conservative treatment. Hematoma of the rectus muscle carries a mortality of 4 per cent.

## SPONTANEOUS HEMATOMA OF THE ABDOMINAL WALL IN PREGNANCY; REPORT OF A CASE

DAVID ROSE

New England J. Med., 234: 582-583, 1946

The literature discloses a total of 31 cases of spontaneous hematoma of the abdominal wall in pregnancy. The hematoma is the result of rupture of the main inferior epigastric artery or one of its branches. Nearly all instances in the literature were in multiparous women of 30 years of age or older. In 18 cases, cough was the causative factor. The hematoma occurred at term in 9 cases and in the last trimester of pregnancy in 12. The most striking feature in the reported cases was the high maternal and fetal mortality, the over-all maternal mortality being 13 per cent and the over-all fetal mortality 16 per cent. Early recognition and appropriate treatment will definitely decrease the mortality rate, since almost all the reported deaths resulted from hemorrhage progressing to severe shock.

The author presents the case of a 36 year old tripara whose past obstetric history was negative. Her present pregnancy proceeded normally in all respects until a week before term when she developed an acute respiratory infection with an associated tracheobronchitis. Three days after the expected date of confinement the patient complained of severe left-sided abdominal pain, nausea and vomiting. Examination revealed the pulse rate to be 78, temperature 98.4 degrees F. and the blood pressure 120/68. The abdomen was nontender and the fetal heartbeat was of good quality at a rate of 132. Adjacent to the left cornu was a small tender mass. There was no spasm or rebound tenderness and no vaginal bleeding or discharge. On the previous day the patient had had severe, sustained spasms of coughing.

Three hours after this examination the pain became so severe that the patient was admitted to the hospital. The temperature was 97.4 degrees F., the pulse 104 and the blood pressure 102/60. The abdominal mass was exquisitely tender with slight muscle spasm. Cesarean section and exploratory laparotomy were decided on. Palpation of the abdominal wall through a midline incision revealed a mass that started 2 fingerbreadths below the costal margin and extended downward. It was obviously a large hematoma in the left rectus muscle with extravasation of blood down through the muscle almost to the crest of the ileum. A cesarean section was performed and 2 grams of sulfanilamide powder was dusted

was found among the general clinic population. The increase in morbidity occurs almost entirely in the group of patients with large myomas. However, it cannot be accounted for on the basis of an increased operative incidence in this group as it is also proportionately higher following abortion and spontaneous delivery.

The fetal mortality among patients in this series was 9.6 per cent compared with that of the general clinic, which is 3.46 per cent. Myoma uteri was undoubtedly a factor in 2 deaths following version and extraction, as it offered definite obstruction to delivery, and it may have been a factor in some of the deaths from prematurity.

There were 3 maternal deaths. The presence of myomas was incidental and entirely unrelated to the cause of death in 2 of the patients.

## HEMATOMA OF THE RECTUS ABDOMINIS MUSCLE: REPORT OF A CASE AND ANALYSIS OF 100 CASES FROM THE LITERATURE

JACOB M. TESKE

Am. J. Surg., 71: 689-695, 1946

The author presents a case of hematoma of the rectus abdominis muscle, and analyzes a series of 100 cases collected from the more recent literature. These cases were classified according to etiology into 4 groups: traumatic (19 cases), cases associated with pregnancy (22 cases), cases occurring during the course of a disease (6 cases), and idiopathic (53 cases).

Hematoma of the rectus muscle, while uncommon in any race, was reported in only 4 cases (4 per cent) in this series of 100 cases, in persons of the colored race. The ages ranged from 17 to 83 years, the average age being 46.8 years.

In the group of 22 cases associated with pregnancy, 16 occurred during pregnancy, 3 during labor and 3 during the puerperium. There was a preponderance of cases in multiparae, especially in those who had had a large number of children.

Only 17 cases in this series were correctly diagnosed before operation; 22 cases were diagnosed as ovarian cyst, 12 cases as appendicitis and 5 cases as ventral hernia. The author states that fewer errors in diagnosis would be made if this condition were kept in mind and given proper consideration in the differential diagnosis.

The most common symptom is pain; it was present in all except 3 cases in this series. A palpable mass was present in 78 cases, tenderness in 71 cases, rigidity in 49 cases, nausea in 23 cases, and vomiting in 15 cases. The average white blood count in this series was 11,600, and the average temperature was 99.5 degrees F. Ecchymosis is a helpful diagnostic sign when present, but it occurs too late to aid in the early diagnosis. It occurred in 21 per cent of the cases, but first appeared on the average of 4 days following the onset of symptoms.

Most cases should be treated promptly by surgery, but traumatic cases in young individuals with healthy musculature of the rectus muscle and a small hematoma do very well with conservative treatment. Hematoma of the rectus muscle carries a mortality of 4 per cent.

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over the uterine incision. It was considered wise not to attempt to empty the hematoma nor to dissect above it to find the bleeder. A dose of 100,000 units of penicillin sodium in 3 cc. of normal saline solution was injected into the hematoma and the abdomen closed. Penicillin was injected intramuscularly in doses of 20,000 units every 3 hours for the next 3 days. The postoperative course was uneventful. Within 24 hours the hematoma was appreciably smaller and it continued to decrease in size until at the end of 2 weeks it was barely palpable. The mother and baby were discharged in good condition.

## EXAMINATION OF THE LOWER UTERINE SEGMENT IN CASES OF SUSPECTED PLACENTA PRAEVIA

ALEX W. SPAIN

Brit. M. J., 1: 761-762, 1946

It is a generally accepted practice that no exploration of the lower uterine segment per vaginam in cases of suspected placenta previa should be made until the operator is gowned and ready to perform cesarean section, if indicated. The author has noted that considerable blood loss may occur between the withdrawal of the examining finger and delivery of the baby by section. The examining technique described in this paper will be found to prevent any serious loss at this time in cases where the cervix has not been taken up.

The method requires the help of a trained assistant. Either the operator or the assistant makes the examination while the other stands ready. The whole or half hand is introduced into the vagina, the middle finger is inserted through the cervical canal and the placenta sought. Should the placenta be found in the lower uterine segment and should section be decided upon, the finger is gently withdrawn. If further placental separation has been caused by the examination, hemorrhage will be immediately apparent. In the event of such hemorrhage the cervix is grasped between the index and middle fingers; very little pressure is needed to close the cervix and check the bleeding. The cervix is held in this manner until the operator has delivered the baby and placenta. Thus, a small limited hematoma will be formed similar to that found in normal third-stage placental separation.

*Results of cases of placenta previa treated by cesarean section*

YEAR	CASE	MOTHERS LIVED	INFANTS		BLOOD TRANSFUSIONS	
			S. B.	N. N. D.	Before examination	After examination
1944	20	20	0	5	0	1
1945	15	15	0	1	3	0
Total.....	35	35	0	6	3	1

This technique has been used at the National Maternity Hospital in Dublin for 2 years. The results are shown in the accompanying table. It will be noted that in only one case was blood transfusion necessary after examination and section. This method is applicable only in cases in which the cervix has not been taken up.

## PATHOLOGY OF LABOR AND PUERPERIUM

### THE CLINICAL DIAGNOSIS OF VARYING DEGREES OF UTERINE CONTRACTION RINGS

HERMAN W. JOHNSON

[Am. Jour. Obst. & Gynec., 52: 74-82, 1946]

In the opinion of the author contraction ring dystocia is rather frequent, being present in the private practice of himself and his associate once in every 80 deliveries; in St. Joseph's Maternity in Houston it was encountered once in every 254 deliveries and in the Memorial Hospital in the same city, once in every 402. He laments the maze of bewildering terminology pertaining to these rings (retraction rings, contraction rings, constriction rings, Bandl's ring, etc.) and prefers to call them all "contraction rings" in conformity with *The Standard Nomenclature of Disease and Operations*. The author believes that rings occur in both obstructed and unobstructed labors and, when present, are always a formidable complication to the progress of labor.

In the first group of cases (obstructed labor), obstruction to the passage of the fetus causes development of the contraction ring, while in the second group the development of a contraction ring causes obstruction to the passage of the fetus. In the first group the ring formation would be dependent on the degree of obstruction to labor. In the second group, and it is this group with which this paper is chiefly concerned, all cases might be divided by their clinical courses into mild and severe. The mild cases would compromise all labors where other causes of dystocia could be eliminated and which greatly exceeded the normal duration, but which terminated spontaneously or by simple delivery procedures under the lower limit of prolonged labor, i.e., 30 hours. The severe cases would comprise labors which greatly exceed 30 hours and terminated under surgical anesthesia by more involved delivery procedures.

The author cannot agree with Rudolph that early rupture of the membranes is not a predisposing factor in the development of uterine rings. It has happened too often in the author's experience to be ignored. In fact, where the membranes have ruptured before or early in labor, and subsequent cervical dilatation has not kept pace with the frequency and severity of the uterine contractions, he has become suspicious of a developing ring and often this suspicion has been warranted.

Many of these patients give a history of the mother having had a long labor. Many of them are introspective and have looked to the very last detail of good prenatal care. As a class, if there be such, they might be called hypertonic inverts. Labor starts quite normally and then after a few hours, the complaints of the patient become urgent because of the colicky nature of the pains. After a few hours of rest produced by sedation, the battle is on again, and as the hours

pass the colicky nature of the pains increases, the patient holds her hands over her uterus because it has become sensitive and she wants to protect it from the hands of doctors and nurses. Meanwhile little progress is made. A vaginal examination may now show the station of the head to be slightly higher than noted earlier in labor with a cervical dilatation of 2 or 3 cm. perhaps and soft, somewhat edematous cervical edges. Now, (as is portrayed in a series of illustrations) the middle finger of the examining hand is inserted rather deeply between the cervix and the head. The other hand is placed on the body of the uterus and kept there until a strong contraction is felt, when the impact on the examining finger is sensed as very weak. The fetal head is found to be movable or loose in the pelvis.

With periods of rest and labor 30 or more hours have now elapsed. "Vaginal or rectal examination may now show the cervix 4 cm. dilated, soft and edematous. The patient is now ready for delivery, and more than likely so per vaginam . . . The edematous cervix is now felt as a drape covering the most dependent portions of the presenting part. It does not require manual dilatation as one thinks of the term, because the cervix generally brushes aside by merely opening and separating the fingers of the operating hand. The latter is now carried upward posteriorly between the lower uterine segment and the fetal head for the purpose of making an accurate diagnosis of position, and also to determine the presence of any loops of cord below the ring. At this time the contraction ring is examined to ascertain what, if any, effect the present degree of anesthesia is having upon its tone. If a loop of cord is not present in the lower uterine segment, a painstaking cephalic application with midplane forceps is made. It may now be desirable, or even necessary, to deepen the anesthesia. Delivery is then effected by careful and steady traction, assisted by gentle pressure on the fundus in the direction of the pelvic inlet. If a loop of cord is present in the lower uterine segment, making it almost impossible for the cord to escape pressure from the forceps' blade, the writer prefers to lift the head up through the dilating or dilated ring, and complete the delivery by version and extraction. Adrenalin chloride will not dilate this type of ring. We tried it many times several years ago and always with the fingers trying gently to find a passage between the ring and the child's body. Ether and chloroform carried to the point of deep surgical anesthesia will relax it."

(Johnson is fully justified in deprecating the varied and confusing terminology which has been applied to the several types of uterine rings. However, it seems questionable whether anything is to be gained by calling them all by the same name since the 3 established varieties are actually quite different in a number of respects. One is physiologic and develops in every labor, another is pathologic in that it is caused by *dystocia* while the third variety is pathologic in that it causes *dystocia*. Our standard textbooks, moreover, now describe these three types and have rather generally agreed upon a simple and logical nomenclature, as follows:

*Physiologic retraction ring.* Due to the phenomenon of retraction the uterus in normal labor becomes divided into an upper and lower segment. At the junction of the two segments there is found a ring, ridge, ledge or rim that has been designated by a number of terms. Since the development of this ring is a normal, physiologic process and since it is the result of retraction, it would seem only natural to call it the "physiologic retraction ring." This

name was first suggested in 1935 by Rudolph, the outstanding American student of the subject, and has been rather generally adopted in this country. (See Rudolph: "Contraction Ring Dystocia," Jour. Obst. & Gynaec. Brit. Emp., 42: 992-1026, 1935.)

The physiologic retraction ring was beautifully demonstrable in an autopsy specimen which I had the good fortune to obtain in the summer of 1945. During the course of a severe poliomyelitis epidemic which swept Maryland that summer, a patient suffering from poliomyelencephalitis who was 7 months pregnant with a twin gestation, died in the second stage of labor from respiratory failure. The thickness of the uterine wall at various levels was measured with meticulous care and the whole specimen carefully drawn to scale. It is reproduced here as Fig. 1. The physiologic retraction ring is clearly seen as a ridge at the lower limit of the upper uterine segment.

*Pathologic retraction ring.* In obstructed labor the process of retraction progresses to an excessive degree and a marked exaggeration of the physiologic retraction ring results. Since this ring is present only in obstructed labors and is due to over-retraction, it has been designated by Rudolph as the "pathologic retraction ring." The term "Bandl's ring" is, of course, so intimately associated with this type of ring that this synonym will doubtless continue in use, but in view of the general tendency to get away from eponyms, it would seem desirable to give preferred usage to the more descriptive term suggested by Rudolph. An example of the pathologic retraction ring is shown in Fig. 2. Here it may be seen that the ring is in no wise obstructing the passage of the baby and this type of ring never impedes the egress of the infant. Contrariwise, it is the result of obstructed labor; and is pathologic also in the sense that it is invariably associated with extreme thinning of the lower uterine segment consequent upon the cephalward rise of the ring. As we all know, the pathologic retraction ring may be seen abdominally in obstructed labor, usually at about the level of the umbilicus, and is one of the classical signs of threatened rupture of the uterus.

*Constriction ring.* This Rudolph defines as "an annular contraction of the uterus which may occur theoretically at any level of the uterine musculature and cause dystocia *per se* in the presence of normal cephalopelvic relationships. It does not change position as labor continues. Rupture of the uterus has never been demonstrated unequivocally to result *per se* from a constriction ring. It is improbable that it would occur because the segment below the ring is not excessively thinned or distended and the uterus above is often relaxed and the contractions are ineffective, that is, a constriction ring is associated with incoordination of uterine action." (See Fig. 3.) Since the word "contraction" is used by Rudolph in his definition of a constriction ring, it is an entirely appropriate term to apply to this condition and Johnson, in the article abstracted above, appears to prefer it. However, the term "constriction ring" seems to be a little more descriptive of what is taking place and since it has found a place in the DeLee-Greenhill and Stander textbooks, it may be regarded as approaching standard nomenclature. Certainly, if we are ever going to get away from the confusion which has long shrouded this subject, we must begin using the same terms and, as I see it, Rudolph's classification is simple and logical and might well be adopted generally.

We have, then, two types of pathological rings: the pathologic retraction ring (Bandl's ring) and the constriction ring. An exceedingly clear differentiation of these two types of ring was published back in 1913 by Clifford White of London (Lancet, 1: 604-607, 1913) and in the belief that it may be helpful to teachers of obstetrics it is reprinted herewith. Rudolph's terminology has been substituted for the older nomenclature used by White.

#### *Constriction Ring*

1. A localized thickening of the wall of the uterus due to the contraction of the circular fibres over a point of slight resistance, most frequently over a depression in the child's outline or below the presenting part.

#### *Pathologic Retraction Ring*

1. The junction of the thinned lower uterine segment with the thick retracted upper uterine segment.

*Constriction Ring*

2. The uterine wall at the site of the constriction ring will therefore be thicker than it is either above or below.

3. The wall below is neither thinned nor over-distended.

*Pathologic Retraction Ring*

2. The uterine wall above the pathologic retraction ring is much thicker than it is below it.

3. The wall below a pathologic retraction ring is both thinned and over-distended.

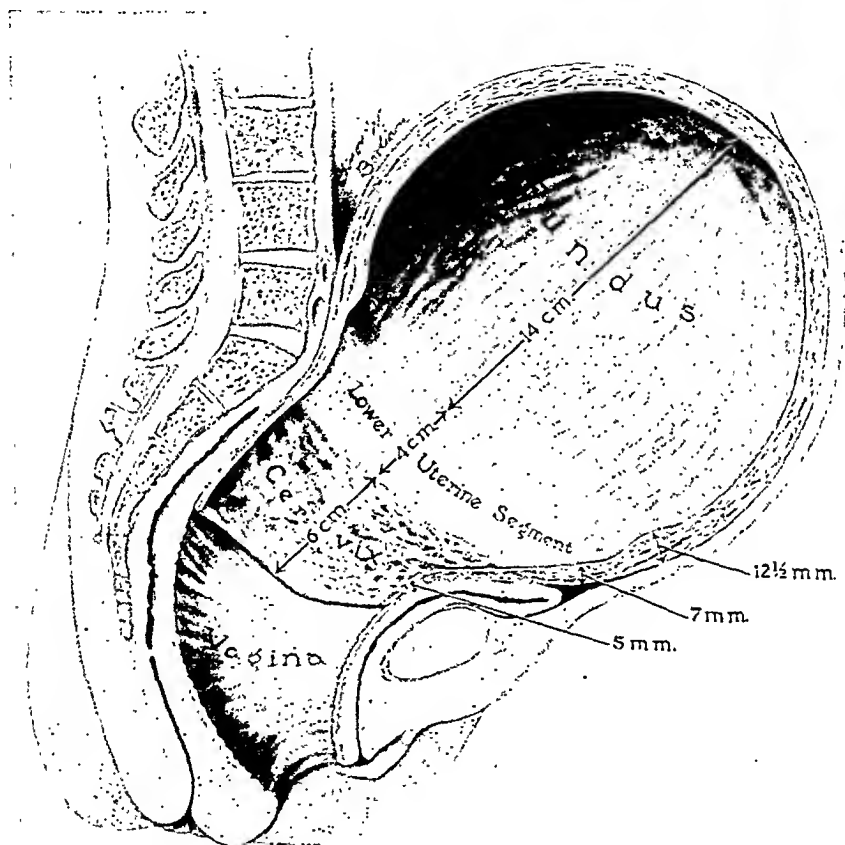


FIG. 1. PHYSIOLOGIC RETRACTION RING, APPROXIMATELY 12.5 MM. THICK, AS FOUND IN PATIENT DYING IN SECOND STAGE OF LABOR OF POLIOMYELENCEPHALITIS  
The twin pregnancy was about 28 weeks in duration

4. The presenting part is not forcibly driven into the pelvis.

5. The child may be wholly or mainly above the constriction ring.

6. The body of the uterus above a constriction ring is usually relaxed and not tender.

4. The presenting part is or has been jammed into the pelvis.

5. Part of the child must be below the pathologic retraction ring.

6. The body above a pathologic retraction ring is tonically contracted and hard.

name was first suggested in 1935 by Rudolph, the outstanding American student of the subject, and has been rather generally adopted in this country. (See Rudolph: "Contraction Ring Dystocia," Jour. Obst. & Gynaec. Brit. Emp., 42:992-1026, 1935.)

The physiologic retraction ring was beautifully demonstrable in an autopsy specimen which I had the good fortune to obtain in the summer of 1945. During the course of a severe poliomyelitis epidemic which swept Maryland that summer, a patient suffering from poliomyelencephalitis who was 7 months pregnant with a twin gestation, died in the second stage of labor from respiratory failure. The thickness of the uterine wall at various levels was measured with meticulous care and the whole specimen carefully drawn to scale. It is reproduced here as Fig. 1. The physiologic retraction ring is clearly seen as a ridge at the lower limit of the upper uterine segment.

*Pathologic retraction ring.* In obstructed labor the process of retraction progresses to an excessive degree and a marked exaggeration of the physiologic retraction ring results. Since this ring is present only in obstructed labors and is due to over-retraction, it has been designated by Rudolph as the "pathologic retraction ring." The term "Bandl's ring" is, of course, so intimately associated with this type of ring that this synonym will doubtless continue in use, but in view of the general tendency to get away from eponyms, it would seem desirable to give preferred usage to the more descriptive term suggested by Rudolph. An example of the pathologic retraction ring is shown in Fig. 2. Here it may be seen that the ring is in no wise obstructing the passage of the baby and this type of ring never impedes the egress of the infant. Contrariwise, it is the result of obstructed labor; and is pathological also in the sense that it is invariably associated with extreme thinning of the lower uterine segment consequent upon the cephalward rise of the ring. As we all know, the pathologic retraction ring may be seen abdominally in obstructed labor, usually at about the level of the umbilicus, and is one of the classical signs of threatened rupture of the uterus.

*Constriction ring.* This Rudolph defines as "an annular contraction of the uterus which may occur theoretically at any level of the uterine musculature and cause dystocia *per se* in the presence of normal cephalopelvic relationships. It does not change position as labor continues. Rupture of the uterus has never been demonstrated unequivocally to result *per se* from a constriction ring. It is improbable that it would occur because the segment below the ring is not excessively thinned or distended and the uterus above is often relaxed and the contractions are ineffective, that is, a constriction ring is associated with incoordination of uterine action." (See Fig. 3.) Since the word "contraction" is used by Rudolph in his definition of a constriction ring, it is an entirely appropriate term to apply to this condition and Johnson, in the article abstracted above, appears to prefer it. However, the term "constriction ring" seems to be a little more descriptive of what is taking place and since it has found a place in the DeLee-Greenhill and Stander textbooks, it may be regarded as approaching standard nomenclature. Certainly, if we are ever going to get away from the confusion which has long shrouded this subject, we must begin using the same terms and, as I see it, Rudolph's classification is simple and logical and might well be adopted generally.

We have, then, two types of pathological rings: the pathologic retraction ring (Bandl's ring) and the constriction ring. An exceedingly clear differentiation of these two types of ring was published back in 1913 by Clifford White of London (Lancet, 1: 604-607, 1913) and in the belief that it may be helpful to teachers of obstetrics it is reprinted herewith. Rudolph's terminology has been substituted for the older nomenclature used by White.

#### *Constriction Ring*

1. A localized thickening of the wall of the uterus due to the contraction of the circular fibres over a point of slight resistance, most frequently over a depression in the child's outline or below the presenting part.

#### *Pathologic Retraction Ring*

1. The junction of the thinned lower uterine segment with the thick retracted upper uterine segment.

*Constriction Ring*

7. Round ligaments are not tense.
8. A constriction ring may occur in the first, second or third stage of labor.
9. A constriction ring does not vary in position as labor goes on.
10. A constriction ring is rarely felt on abdominal examination.
11. The patient's general condition is good.
12. Causation: premature rupture of the membranes; intrauterine manipulations.

*Pathologic Retraction Ring*

7. Round ligaments stand out.
8. A pathologic retraction ring practically always occurs late in the second stage of labor.
9. A pathologic retraction ring gradually rises as retraction of the upper uterine segment proceeds.
10. A pathologic retraction ring may frequently be felt per abdomen.
11. The patient's general condition is bad.
12. Causation: obstructed labor.

Returning now to Johnson's paper, one of the curious things about constriction rings (or "contraction rings") is the wide discrepancy in their reported frequency. Johnson encountered them 126 times in 10,000 private patients, or once in every 80 cases. On the other hand, Rudolph who has likewise been on the lookout for them and has had a huge material at his disposal at the Cook County Hospital in addition to private practice, was able to report only 26 cases of his own in 1935, and could collect from the entire world's literature but 371 cases, or 3 times as many as Johnson has seen in private practice. Johnson explains this on the grounds that Rudolph's series comprised only severe cases while his included many mild ones. Certainly, our standard text-books do not give the impression that it is a very frequent complication, and in the detailed annual reports of our large obstetrical clinics the condition is rarely even cited in the lists of complications. At the Hopkins Hospital we make this diagnosis once in every 2000 cases or so, and then usually put a question mark after it.

How are we to account for this glaring discrepancy? There are several possible explanations. Having good reason to respect Johnson's clinical acumen, I want to state as the first possibility that he may be entirely correct. This would mean that most of the rest of us, through lack of awareness of constriction rings, are overlooking a huge number of them. A second possibility is that the majority of the cases he describes, particularly those he calls mild, fall into the category which is ordinarily referred to as uterine inertia. He does not state whether or not the uterus was indentable at the acme of a pain in these cases, but it would be my suspicion that it probably was in many of them. This does not rule out, of course, the presence of an associated constriction ring, but in that event the burden of proof would seem to rest with the person who says that such existed; and as far as I can gather, Johnson did not attempt to palpate the ring in these mild cases. In regard to his severe cases,—the labors which lasted over 30 hours and in which the cervix was "brushed aside" and mid-forceps applied,—these sound very much to me like the cases which we regard as intractable uterine inertia and in which we are finally forced to give up and perform either Dührssen's incisions and forceps or extra-peritoneal cesarean section. We may have missed some rings in these patients, but how often do such cases occur? In our last 6000 deliveries we have performed 5 Dührssen's and 8 sections because of intractable uterine inertia,—a total of 13 cases, or one in every 452 deliveries. This is as far as I would venture to go in any concession on the frequency of actual constriction rings and this may be going too far.

A third, and possibly the best, explanation of the discrepancy in the recorded incidence of constriction rings, is a sort of a compromise between the two foregoing explanations. It may be that the cases which Johnson describes, and which in our clinic would be called uterine inertia, are both examples of inco-ordinated muscular behavior in which the autonomic and sympathetic nervous act antagonistically so that the expulsive forces of the longitudinal muscle fibers of the fundus are resisted by the circular muscle bundles of the lower segment which, instead of relaxing as they are supposed to do, are continually contracting.

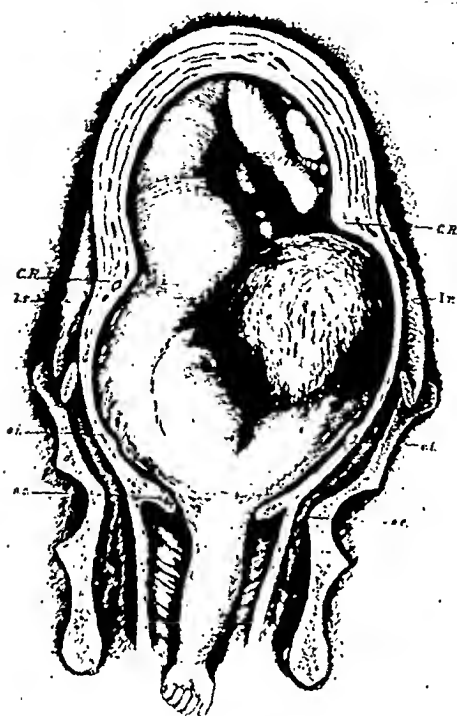
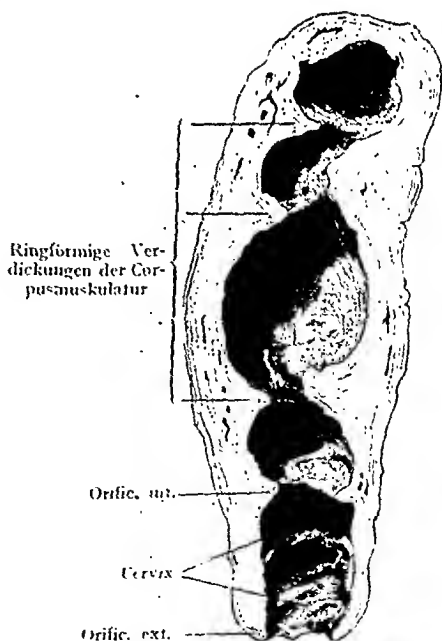


FIG. 2. PATHOLOGIC RETRACTION RING, MARKED C. R.  
(FROM SCHROEDER)

FIG. 3. MULTIPLE CONstriction RINGS IN POSTPARTUM UTERUS REPORTED BY BUMM AND BLUMREICH.

Two definite constriction rings divide the upper uterine segment into 3 cavities. Below, two probable constriction rings are present: one at the junction of the upper and lower segments and another at the internal os. The uterus is normally retracted.



*Constriction Ring*

7. Round ligaments are not tense.
8. A constriction ring may occur in the first, second or third stage of labor.
9. A constriction ring does not vary in position as labor goes on.
10. A constriction ring is rarely felt on abdominal examination.
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(See editorial note on article by G. Diek Read, August issue of Survey, page 461.) Since the crux of the difficulty here would be the constricting action of the circular fibers of the lower segment, it would be possible to regard this in the light of ring formation even though the ring could not be actually palpated in most cases.

Finally, to turn to a different and more practical aspect of this paper, there is one feature of it which strikes me as most disturbing, namely, the recommendation that interference be carried out in some of these cases when the cervix is only 4 cm. dilated, this to be done by "wiping aside" the cervix and applying mid-forceps. With careful selection of cases and in Johnson's skilled hands, this procedure doubtless yields satisfactory results, but if it is copied by practitioners at large throughout the country, the outcome is certain to be disastrous. *In the cases of failed forceps which are referred to our clinic for delivery, the cervix on admission is less than 7 cm. in more than 85 per cent.* And the country over, these premature forceps attempts prior to complete dilatation constitute one of the most common and costly of obstetric errors. Hence my concern over any recommendation which might be interpreted as condoning this practice.—(Ed.)

## AN EVALUATION OF THE TREATMENT OF THE PERSISTENTLY UNENGAGED VERTEX IN THE MULTIPARA

M. D. SPEISER AND G. SPECK

Am. J. Obst. & Gynec., 51: 607-620, 1946

In the present paper, the authors attempt to evaluate the causes for lack of engagement and the use particularly of version and breech extraction for this condition in the multiparous patient.

The conditions which act against engagement are either of a functional or pathologic nature. Those of a functional nature include the following:

1. Relaxed abdominal wall of a multipara may permit a faulty direction of the fetal axis and uterine forces. Faulty positions and presentations are also favored. These circumstances may cause delay in engagement which may subsequently be overcome.
2. A large distended bag of forewaters may prevent engagement prior to its rupture.
3. Presence of an absolutely or relatively short cord may cause delay in engagement.
4. Delay in engagement may occur in patients who are physically poorly prepared for labor, due to insufficient rest, anemia, etc.

The pathologic factors preventing engagement may be: cephalopelvic disproportion, unretracted fibroids obstructing the pelvic inlet, extrauterine neoplasms, placenta previa, or monstrosities such as hydrocephalus.

In order to evaluate the results of version and breech extraction for persistently unengaged vertices, the authors have studied the cases of 21 multiparas delivered by this procedure. The indications for version and breech extraction were as follows: lack of progress, 9 cases (secondary uterine inertia in 6 of these); maternal distress, 2 cases; fetal distress without an associated prolapsed cord, 2 cases; prolapse of the cord, 8 cases.

In this series, there were 9 babies born dead and 3 died shortly after delivery, an uncorrected fetal mortality of 57.1 per cent. It was felt that in 8 cases the method of delivery was a factor in the production of the stillbirths, giving a corrected fetal mortality of 38 per cent. There were 2 maternal deaths, an incidence of 9.5 per cent. In one case, where secondary uterine inertia was present, an attempt at forceps delivery was made, and a contraction ring added to the complications. Delivery was accomplished by a difficult version and breech extraction resulting from a definite cephalopelvic disproportion which was not recognized. After delivery the patient went into shock and died on the 31st postpartum day from thrombosis of the left pulmonary artery and lung infarction. In the second maternal death, version was attempted and a contraction ring was noted. Under ether anesthesia and adrenalin, version was easily performed. Breech extraction was performed, with difficulty in delivery of the shoulders, and a stillbirth resulted. The cervix was lacerated, blood loss was 2000 cc. and death followed in 4 hours.

The authors conclude that version and breech extraction, per se, cannot be condemned, since in 9, or 42.9 per cent, of the cases in which no other complications existed, the results were satisfactory. However, there is a tendency to perform version and breech extraction without thorough investigation of the causes for the persistent lack of engagement, which factors may constitute contraindications for this procedure. The failure to recognize cephalopelvic disproportion accounted for 50 per cent of the fetal deaths. In the presence of failure of engagement in the multipara, therefore, version and breech extraction should not be performed until there is absolute proof that no disproportion exists. The presence of a residual rim of cervix may be a very definite hazard in the performance of version and breech extraction. Version may be safely executed but the breech extraction deferred until the cervix offers no obstruction.

Upon recognition of cephalopelvic disproportion, cesarean section is the procedure of choice. The authors cite 22 such cases in which there was but one fetal death (4.5 per cent) and no maternal deaths.

(The best treatment of the persistently unengaged vertex, in the absence of disproportion, is TIME.—Ed.)

## SOME POINTS IN THE AETIOLOGY AND MECHANISM OF OCCIPITO-POSTERIOR POSITIONS

J. W. JOHNSTONE

M. J. Australia, 1: 531-532, 1946

Academically, it is the custom to divide the pelvic brim into 4 quadrants, and to define the 4 vertex positions accordingly as the occiput lies to the right or left of the sagittal plane and in front or behind the coronal plane. The smooth forward curvature of the mother's anterior abdominal wall accommodates more

readily the fetal back and favors the anterior positions. In the fewer cases in which the fetal back is behind, it tends to be extended by the forward projection of the opposing lumbar part of the maternal spine. This forward projection also pushes the fetal torso to one side and thus accommodates it more conveniently in the oblique diameters.

The author discusses the mechanism of presentation of the head under 3 headings: engagement, transit and rotation and disengagement. Referring to engagement, it is the usual teaching that the head engages in the oblique diameter with the occiput posterior in about one-fourth of the cases. Recent x-ray studies before and during labor have led to a revision of this teaching. The actual diameters of engagement of the head as it settles into the brim depart radically from the 2 geometrical obliques. It has been pointed out that a directly anterior or posterior presentation of the occiput is not uncommon, while in the majority of cases the head negotiates the brim approximately in the transverse diameter.

During transit of the head through the cavity, 3 things can happen. First, the occiput can take the long rotation to the front to be delivered in the normal manner. Secondly, it can remain arrested at or behind the transverse diameter. Thirdly, it can be deflected to the back and delivered as a persistent occipito-posterior presentation. Extension of the head is a prime factor in posterior positions of the occiput in bringing the sinciput lowermost and thus deflecting the occiput to the sacrum. As the normal transverse diameter of the cavity is about  $4\frac{1}{2}$  inches, there might be a mechanical barrier to forward rotation should the occiput have entered behind the transverse diameter. This is particularly true with the android type of pelvis.

Disengagement of the head from a persistent occipito-posterior presentation occurs first by the fixation of the root of the nose against the lower symphysis, the head thus put in flexion and the perineum allowed to slip over the occiput. The degree of flexion is determined by the amount of space in the bony outlet. Thus, the head is engaged first by flexion and the disengagement completed by extension. In the forceps delivery of a fetus presenting persistently in the occipito-posterior position, there is a mechanical disadvantage in that the pull of the axis traction is directed forward onto the pubis and tuberosities, and also that instead of allowing the primary movement of flexion to occur, it tends to pull the head into premature extension. This is one of the factors accounting for the 50 per cent fetal mortality at this hospital when the occipito-posterior presentation requires forceps, as compared with a 12 per cent fetal mortality rate when spontaneous delivery occurs.

The author discusses the various types of pelvis and the birth sequences which often occur with each type. Attention is also drawn to the relationship between the pelvic type and general physical characteristics and body habitus.

THE MANAGEMENT OF THE OCCIPITO-POSTERIOR  
PRESENTATION

W. I. HAYES

M. J. Australia, 1: 532-534, 1946

Discussing the management of occipito-posterior positions before labor, the author believes that Buisst's method of correction by means of abdominal pads and binder can often be effective when rectification is most desirable. The method is indicated only in primiparae at the end of pregnancy when the fetal occiput is unfixed in the posterior position.

Referring to management during labor, when delay occurs early in labor the head is incompletely flexed and remains unfixed with the occiput directed posteriorly. The possibility of disproportion great enough to justify cesarean section should be kept in mind. Eventual fixation, followed by slow and continuous descent eliminates the possibility of insuperable disproportion and vaginal delivery may then be expected with confidence. When delay occurs toward the end of the first stage of labor, deflexion of the head often causes an arrest when the cervix is not fully dilated. Manual rectification under general anesthesia to an anterior position is indicated and is carried out by gently pushing up the head vaginally, and then passing the hand behind the head up to the posterior shoulder which is brought across the mid-line. The other hand is used externally to push the anterior shoulder in the opposite direction. When the shoulders are brought in the opposite oblique diameter of the pelvis, the head, with occiput leading, is brought down into its new position by the internal hand, and the patient is allowed to continue in labor. When the head has passed through the fully dilated cervix and occupies the pelvic cavity, delay may be caused by its failure to rotate from the posterior position, by partial rotation to the position of "deep transverse arrest," or by adverse rotation of the occiput to the sacrum. The treatment of these 3 conditions is by manual rotation, the application of forceps and delivery. In cases in which there is a transverse contraction in the pelvic outlet, it is probably safer to avoid rotating a head in the occipito-posterior or occipito-sacral, and to deliver the child with forceps in the face-to-pubes position, after performing a deep episiotomy.

Delay with the head on the perineum in an occipito-sacral position is the result of a resistant perineum and of the inability of the flexed head in the occipito-sacral position to flex sufficiently far to pass forward under the pubic angle. The treatment is to deliver the fetus with forceps in the posterior position, assisting the natural mechanism and using a deep episiotomy.

The author discusses at length rotation with forceps in occipito-posterior presentations, stressing that this operation should be reserved for the expert.

## MANAGEMENT OF OCCIPITO-POSTERIOR POSITION

SUBODH MITRA

Calcutta M. J., 43: 44-47, 1946

Ninety per cent of all occipito-posterior cases (which form only 10 per cent of all vertex presentations) deliver naturally without any complication; however, the author believes that there exists a too complacent attitude in respect to posterior position cases. The diagnosis in the group which do present difficulty is not entirely easy and is often made late by noting the delay and prolonged nature of the labor. An examination of statistics at 2 local maternity hospitals reveals that during the last 5 years, out of 15,553 confinements, 364 were occipito-posterior cases, or an incidence of 2 per cent. Of the 364 occipito-posterior cases, 213 delivered naturally, while 151 (41 per cent) required instrumental delivery. There was an incidence of 2.2 per cent of maternal mortality and 16.2 per cent of fetal mortality. The incidence of both maternal and fetal mortality is definitely higher than that of average vertex cases.

In the progress of an occipito-posterior case, during the first stage of labor the cervix will resist dilatation. The patient becomes exhausted on account of the strain of long, continued ineffectual pains. This stage should be carefully tided over with sedatives and maintenance of nutrition. In the absence of disproportion, nature will ultimately yield and the second stage begin. In those cases where the cervix will not dilate after rather indefinite waiting, intervention will be required. The author chooses to dilate the cervix manually under gas and oxygen anesthesia.

In the second stage, difficulties are experienced because of persistence of oblique position, deep transverse arrest or short rotation to the hollow of the sacrum. Without intervention, some of the posteriorly rotated cases may be born naturally in a face-to-pubis position, provided that the head is comparatively small and the expulsive force strong. Persistent occipito-posterior and deep transverse arrest conditions require interference unless the head should rotate either anteriorly or posteriorly. Methods of extraction are: internal podalic version, forceps extraction with or without manual rotation, cesarean section and craniotomy. The author believes that internal podalic version should be done only under exceptional circumstances and that forceps extraction after manual rotation is the operation of choice. Those cases where manual rotation is possible can very well be rotated with forceps during the process of extraction. A frank case of occipito-posterior position should on no account require a cesarean section unless such disproportion exists as would justify it irrespective of the position of the child. Lastly, in cases where the uterus is firmly retracted over the child or where there is a contraction ring grasping the neck and the child will invariably die, it is best to do a craniotomy.

In conclusion, the author states that in the management of an occipito-

posterior position, one loses more by too early interference than by too long expectancy. Tact, careful vigilance, proper judgment as to when to interfere and perfect obstetric acumen are the 4 cardinal points to make the whole operation a success.

## HAEMOLYTIC STREPTOCOCCI IN PUERPERAL SEPSIS

J. DICK

Edinburgh M. J., 53: 134-138, 1946

In examining high vaginal swabs from women showing pyrexia during the puerperium, only 51 per cent of the beta-hemolytic streptococci isolated over a period of 2 years were found to be group A. Therefore, the present study was undertaken to determine the incidence of groups B, C, G and D in these cases. Beta-hemolytic streptococci (those showing a hemolytic zone on blood agar plates) were tested also for soluble hemolysin (using washed human cells), for fibrinolysin and as to their biochemical reactions.

One hundred strains from high vaginal swabs were isolated and examined, while the results obtained with 167 other beta-hemolytic strains from various sources, chiefly throat swabs, were studied for purposes of comparison. The high vaginal swabs were taken from patients showing degrees of puerperal sepsis varying from trivial to severe. Forty-eight per cent of the 100 strains from high vaginal swabs proved to be group A; 16 per cent, group B; 10 per cent, group C; 8 per cent, group G; 9 per cent, group D; and 9 per cent did not fall into any of these groups.

The formation of a soluble hemolysin by the streptococci of groups A, C and G is evidence of the presence of an exotoxin, while the positive fibrinolytic test with 100 per cent of the group A strains, 90 per cent of the group C strains and 50 per cent of the group G strains is proof of the invasive power of these strains.

The power of the groups C and G strains, like those of group A, to ferment trehalose and not sorbite is further evidence of their human origin. The fact that in 3 of the group C and 3 of the group G cases the growth of streptococcus was a pure one is corroborative evidence of etiological connection between the organism and the condition of sepsis. The evidence for the pathogenicity of the groups B and D strains is not so strong, with an absence of a strong hemolysin and of fibrinolytic activity. Nevertheless, the presence of these strains in pure culture in 6 instances with group B and one with group D suggests that they may cause a lower grade of sepsis. One strain not falling into any of these 5 groups was also obtained in pure culture.

Fermentation tests with trehalose and sorbite are helpful in differentiating between "human" strains of groups B and G and those of animal origin. Starch

and glycogen were found in this series to have a limited use in differentiating between group A and groups C and G.

The author's clinical analysis is based upon the duration of hospital stay of most of these cases. The average hospital stay after the onset of fever was 11 days for group B; 16 days for group C; 12.5 days for group D; and 10 days for group G. The average stay of the cases yielding hemolytic streptococci which did not fall into any of these groups was 6 days. While group A streptococci are the undoubted important bacteriological factor in severe puerperal sepsis and septicemia, streptococci of groups B, C, D and G are also associated with an appreciable number of cases in which the sepsis is usually less severe. The above clinical evidence suggests that group C infections were, after group A, the most severe, and the ungroupable streptococci the least severe; with groups D, B and G cases occupying intermediate positions.

## POST-ABORTIONAL TETANUS WITH RECOVERY

JEAN HUTCHINGS AND ALICE WHEILDON

M. J. Australia, 1: 404-406, 1946

According to the literature, although the incidence of post-abortion tetanus is low, the mortality is high, averaging 84 per cent. The authors present a severe case in which the patient recovered.

A 27 year old woman was admitted to the hospital 5 days after having syringed herself with a soap solution, procuring the abortion of a fetus. On the morning of her admission she noted stiffness of the neck and jaw which progressed and became painful, so that upon admission she was unable to turn her head or open her mouth. On examination the sternomastoid muscles were standing out like cords and extreme pain and stiffness, made worse by movement, were present in the neck. The heart and lungs appeared normal and there was no abdominal rigidity. The blood pressure was 180/90, temperature 99.4 degrees F., pulse 104 per minute and respirations 22. The uterus was enlarged to the size of an 8 week's pregnancy, no pelvic tenderness was present, and the lochia were not offensive.

Treatment was instituted 5 days after the introduction of infection and 14 hours after the onset of symptoms. Sedation was begun with rectal paraldehyde and 100,000 international units of tetanus antiserum were administered intravenously in normal saline drip infusion. During this time a bacteriological diagnosis of tetanus was made. When the administration of serum was complete, curettage was performed and a large amount of clean-looking placental tissue removed. Thereafter treatment included prevention of spasms by adequate sedation, specific treatment with antitoxin, prevention of bronchopneumonia and the maintenance of adequate nutrition.

The authors discuss the advantage of curettage after adequate treatment with antitoxin. While curettage cannot be expected to remove the organisms which have already invaded the uterus, it will reduce the danger of hemorrhage and secondary infection and, given adequate amounts of circulating antitoxin, there should be no danger from such a procedure.

"Sodium Amytal" appeared to be an effective agent for the control of spasms. Strenuous measures were taken in the prevention of bronchopneumonia, postural drainage being an important factor. The patient had completely recovered 34 days after the onset, and was discharged from the hospital 47 days after admission.

## THE NEWBORN

### CONGENITAL ABNORMALITIES IN INFANTS FOLLOWING INFECTIOUS DISEASES DURING PREGNANCY, WITH SPECIAL REFERENCE TO RUBELLA: A THIRD SERIES OF CASES

CHARLES SWAN AND A. L. TOSTEVIN

M. J. Australia, 1: 645-659, 1946

The present investigation concerns a series of 58 cases. Forty of these patients had rubella in pregnancy and 2 contracted German measles less than a fortnight prior to conception. The remaining 16 patients suffered from other infectious diseases during pregnancy, including morbilli (8 cases), mumps (3 cases), chicken-pox (2 cases), herpes zoster (2 cases) and scarlet fever (one case). Of the resulting 56 infants and 2 fetuses examined, 46 were found to have congenital malformations.

In the 40 instances where the mothers had suffered from rubella during pregnancy, 36 of the infants and one fetus exhibited congenital defects. The abnormalities comprised 11 cases of deaf-mutism; 11 cases of deaf-mutism and heart disease; one case of deafness and heart disease; one case of deaf-mutism, heart disease and strabismus; one case of deaf-mutism, cataract and heart disease; one case of deaf-mutism and nevus; one case of speech defect and heart disease; one case of cataract and lack of closure of the fetal fissure; 2 cases of heart disease; one case of mongolism and heart disease; one case of microcephaly; one case of microcephaly and backwardness in development; one case of cleft palate; one case of *spina bifida occulta*; one case of heart disease and hypertrophic pyloric stenosis; and one case of spastic diplegia, hypertrophic pyloric stenosis, inguinal hernia and strabismus. In addition, in a further 18 of the foregoing cases microcephaly was also present. Four of the mothers had had German measles in the first month of pregnancy, 19 in the second month, 8 in the third month, 2 in the fourth month and one in each of the fifth, sixth and eighth months; in the remaining case the duration of pregnancy at the time of the infection was not determined. In the 3 cases in which the infant born subsequently was normal, the mothers had contracted the disease in the second, fourth and sixth months of pregnancy, respectively.

In the 2 instances in which rubella had been contracted less than a fortnight before conception, the offspring were apparently normal.

Of the 8 cases of morbilli during pregnancy, 2 of the babies were born with congenital defects. One child suffered from pyloric stenosis and a suggested heart lesion, while the other had *genu valgum*. The mothers of both of these babies had morbilli in the fourth month of pregnancy. Of the 3 cases of mumps, all babies had defects: one had a slight capillary nevus of the eyelid, in one a true anus was absent, the large intestine terminating inside the *labia majora*, and in

one the head circumference was slightly below normal. Two of the 3 mothers had contracted mumps in the first month and one during the seventh month. The 2 mothers who had chicken-pox contracted the disease in the seventh month of pregnancy and one of the infants had a nevus of the scalp and signs suggestive of a cardiac defect. The 2 mothers who had *herpes zoster* had contracted it in the fourth and sixth months, respectively. Both infants exhibited congenital defects, one had deaf-mutism, microcephaly and heart disease, and one suffered from a myelocoele, bilateral talipes and right *genu recurvatum*. One woman who had scarlet fever when 7 months pregnant gave birth to a child which died at the age of 5 weeks from congenital obliteration of the bile ducts.

The authors discuss the pathogenesis of the anomalies in the light of the experiments of Stockard, and conclude that, while congenital abnormalities most often follow when the mother has had rubella in the first 3 months of pregnancy, the contraction of rubella in the fourth month is relatively often followed by congenital malformations. Also, it is suggested that an attack of rubella in the very early months of pregnancy is not invariably followed by the presence of congenital defects in the child. The fact that many of the children suffering from congenital defects as a result of maternal rubella also exhibit stunting of growth, indicates that as well as the main attack of the virus upon the special cells of certain primordia, there is a general but much slighter attack upon the less-specialized cells of the skeletal tissue.

## ABORTION FOR PROBABLE DEFECTS IN THE CHILD

Lancet, 1: 208, 1946

The suggestion that, when a woman contracts rubella in the early months of pregnancy, abortion should be induced to prevent the birth of a defective child raises an interesting legal point. The fact remains that abortion is a statutory felony under the Offences against the Person Act, 1861. In 1929 the Infant Life (Preservation) Act introduced an amendment in which there was an important proviso—"no person shall be guilty of an offence under this section unless it is proved that the act which caused the death of the child was not done in good faith for the purpose only of preserving the life of the mother."

At present, it may be considered established that the burden is on the prosecution to prove beyond reasonable doubt that the surgeon did not operate in good faith to preserve the mother's life and further, that those words "for the purpose only of preserving the life of the mother" are to be construed "reasonably." They do not mean only that he operates because the mother's life is in instant danger but they protect the surgeon if continuing pregnancy would mean that the "patient became a physical and mental wreck." If a woman can be assured that her child is certain to be born with some terrible deficiency, it might well have a deleterious effect on her mind.

In this field of law borderline cases are to be expected. All that can be said is that the termination of pregnancy is still prima facie a felony, but that juries are often sympathetic.

## NOTES ON THE PATHOGENESIS OF CONGENITAL HEMOLYTIC DISEASE (ERYTHROBLASTOSIS FETALIS)

ALEXANDER S. WIENER

Am. J. Clin. Path., 16: 319-321, 1946

The author discusses some of the puzzles in the pathogenesis of congenital hemolytic disease, and of intragroup transfusion incompatibility. Several of these problems are presented below.

*The development of jaundice and anemia often severe enough to cause death within a few hours or days in infants apparently normal at birth:* Conglutinin (X protein) appears to be a complex of albumin, globulin, phospholipid, perhaps with some fibrinogen, which is absorbed by antigens after they have been sensitized by their specific antibodies. X protein causes the sensitized red cells to stick together and brings about slow hemolysis of the red cells. The author's theory is that only the simple precursors of X protein are present in the fetus, but the physiologic changes occurring after birth (cooling of the skin, dehydration) cause these to aggregate into larger molecules of conglutinin, thus accounting for the frequently delayed onset of congenital hemolytic disease until after birth.

• *The role of A and B factors in congenital hemolytic disease:* The natural anti-A and anti-B agglutinins are believed to be composed of large molecular aggregates. Only when individuals of genotype Kk (or KK) become strongly sensitized are sufficient univalent A and B antibodies formed, which can traverse the placenta more readily. Congenital hemolytic disease occurring in this manner may be clinically indistinguishable from disease caused by Rh sensitization; usually, however, the A-B-O are milder.

*The almost invariable escape from congenital hemolytic disease by the first born, unless the mother has been sensitized by a previous injection of Rh-positive blood:* During pregnancy chorionic villi may become detached, but the fetal red cells in them are usually too few to sensitize any but the rare individuals of genotype KK. However, during labor and delivery, presumably larger numbers of fetal cells gain access to the maternal circulation due to disturbances at the placental site.

*The occurrence of congenital hemolytic disease when the mother is Rh-positive:* Such cases are explained by sensitization to the A-B factors, by sensitization of mothers of one Rh blood type to blood of a different Rh blood type, or by sensitization to the Hr factor, etc.

*The manifold clinical manifestations of congenital hemolytic disease:* The different clinical manifestations of the disease may be correlated with variations in the quantity and quality of the antibodies in the maternal serum. A large amount of univalent antibody passing into the fetal circulation during pregnancy may result in a stillbirth (hydrops), while when only weak univalent antibodies are present, the infant will usually be born alive with anemia. The bivalent antibodies apparently gain access to the fetal circulation mainly during labor and delivery. In these cases there results damage to the liver and brain in a deeply jaundiced infant with little or no anemia.

The author reports findings which indicate that at least one variety of spina bifida is produced by Rh sensitization.

## PATHOGENESIS OF KERNICTERUS

A. S. WIENER AND M. BRODY

Science, 103: 570, 1946

The authors present their concept of the pathogenesis of kernicterus (jaundice of the nuclear masses of the brain), based on recent clinical, serological and pathological observations. Until recently, there was no explanation for the post-mortem finding of kernicterus only in cases of icterus gravis neonatorum, and not following other types of jaundice, even of severe degree.

The role of the Rh factor in congenital hemolytic disease is briefly discussed. In the authors' experience, when the complication of kernicterus supervenes, the antibodies in the maternal serum are almost always of the bivalent variety (agglutinins). This suggests the following mechanism for the development of kernicterus. Maternal Rh agglutinins in the infant's circulation combine with its Rh-positive erythrocytes, bringing about the formation of small clumps (agglutinates of red cells) which plug the smaller arterioles with the formation of agglutination thrombi. In the brain, plugging of terminal vessels can produce areas of ischemic infarcts; the nuclear masses would be the most vulnerable, since ganglion cells are particularly susceptible to anoxia. Due to the concomitant presence of deep jaundice, the damaged ganglion cells take up bilirubin—a sort of *in vivo* staining reaction. Should the infant die at this point, post-mortem examination will show the presence of kernicterus. Infants surviving the immediate neonatal period and dying after the jaundice has disappeared will show at post-mortem examination evidence of cerebral damage but without kernicterus.

Infants with kernicterus occasionally survive, in which case they develop signs of a diffuse neurologic disorder of varying severity, usually accompanied by mental deficiency. Such cases are rare and would be expected to constitute only a small fraction of the group of so-called nonspecific mental deficiency cases.

Attempts have been made to show a connection between Wilson's disease and kernicterus. The authors have studied 3 cases of Wilson's disease, and found in these no evidence of isoimmunization of pregnancy, indicating a dissimilarity in the pathogenesis of the 2 conditions.

## TREATMENT OF SEVERE ERYTHROBLASTOSIS BY SIMULTANEOUS REMOVAL AND REPLACEMENT OF THE BLOOD OF THE NEWBORN INFANT

HARRY WALLERSTEIN

Science, 103: 583-584, 1946

Many babies with erythroblastosis have died of the disease, though no evidence of severe anemia existed. A factor of toxemia, possibly arising from the stromal substance of the lysed red blood cells, undoubtedly plays an important part in the fatal outcome of these cases. Manifestations of such a toxemia are found in kernicterus and in evidences of kidney and liver damage. The author felt that the mere administration of Rh-negative blood did not meet the problem in all cases, it seeming desirable to remove the known Rh-positive blood of the infant and to replace it with Rh-negative blood. Such a procedure would minimize or entirely prevent the action of hemolytic and products upon the liver, kidneys and brain ganglia.

This purpose is carried out to a considerable degree by the simultaneous withdrawal of the Rh-positive blood from the sagittal sinus and the administration of Rh-negative blood through a cannulated vein. The author demonstrates that, inasmuch as the child is given approximately 100 cc. of Rh-negative blood over and above that withdrawn, the dilution factor permits of a reduction of the original Rh-positive blood to 25 per cent of the original volume. This has been confirmed by the typing of blood cells before and after the procedure.

This technique has been carried out on 3 infants who were severely ill with erythroblastosis, with immediate improvement in their conditions and eventual recovery without further therapy. Such results justify a more widespread use of this method in combating severe cases of erythroblastosis fetalis.

## ADRENAL HAEMORRHAGE IN ERYTHROBLASTOSIS

REGINALD WEBSTER

M. J. Australia, 1: 163-164, 1946

The author discusses the occurrence of bilateral severe and devastating adrenal hemorrhage as a concomitant of erythroblastosis fetalis. In one particular case

the infant showed neonatal jaundice and the laboratory findings indicated an extreme degree of erythroblastosis. The mother's obstetric history was consistent in that her first and only other child had been jaundiced at birth but eventually recovered. The red cells of the father and present baby were Rh-positive and those of the mother Rh-negative. Autopsy of the infant revealed adrenal hemorrhage from which not a pin-point of glandular tissue appeared to have escaped. Fluid blood escaped on incision of the capsule of one of the adrenals and it was evident that the glandular tissue was totally disintegrated. It is the author's opinion that the adrenal apoplexy was referable directly to the congenital hemolytic anemia and its associated hemorrhagic tendency.

In connection with the subject of erythroblastosis the author discusses 2 cases in which the Rh situation deviated from that usually found. In each case erythroblastosis was well attested by laboratory and autopsy findings. In one instance mother and baby were both of blood group O and the blood of both was Rh-positive. In the other, both were of blood group A and their blood was Rh-positive. In these circumstance it is suggested that the iso-immunization which precipitated fatal *icterus gravis* in these 2 infants was based on differences in Rh subtypes prevailing in the respective mothers and their babies.

## CENTRAL NERVOUS SYSTEM RESISTANCE; THE EFFECTS OF TEMPORARY ARREST OF CEREBRAL CIRCULATION FOR PERIODS OF TWO TO TEN MINUTES

ROBERT G. GRENELL

J. Neuropath. & Exper. Neurol., 5: 131-154, 1946

A review of the literature reveals that although several investigators have reported effects of cerebral anemia, they were not able to produce a complete anemia and their results are variable. It is also noted that other types of deficiency in substances normally brought to the brain, such as hypoglycemia, vitamin B deficiency, inanition, CO poisoning, etc., often produce lesions in the brain which, in many instances, resemble those resulting from the present experiments.

In this study, adult dogs were subjected to periods of complete arrest of cerebral circulation for periods of 2, 4, 6, 8 and 10 minutes. Observations were made during and following the arrest of brain circulation. The animals were sacrificed and the brains were sectioned, cut and stained in order that the effects of complete cephalic stasis on the various areas of the brain might be studied.

The course of recovery following 2, 4 or 6 minutes of cephalic stasis is practically identical except for differences in time relation dependent on the duration of stasis. Reflexes return in regular order after restoration of blood flow to the brain and a gradual passing off of spinal shock. Following the return of function of vital centers, for a period the dog lies in deep coma with hyper-irritable re-

flexes and continuous vigorous motion of all 4 limbs. The period of hyperactivity persists for several hours and is followed by a period of quiescence with no spontaneous movements. Visual, auditory and olfactory sensations appear to be absent and the touch and pain thresholds are elevated. There is an absence of righting reflexes and vestibular function and a statue-like rigidity. Respiration is normal but the heart rate is slow and shows a marked respiratory arrhythmia. Consciousness eventually returns.

However, consciousness is never restored in animals which survive periods of complete cephalic stasis of 8 minutes or longer. Such an animal shows apparently permanent loss of sensations of vision, hearing and smell and an increased pain threshold. There is complete disappearance of vocalization and of emotional reactions. Spontaneous movements are extremely infrequent and restricted.

The author summarizes the microscopic observations as follows:

1. Beyond some variation from case to case, a definite trend of increase in intensity of injury and number of susceptible areas can be observed in brains subjected to circulatory arrest of from 2 to 10 minutes.

2. Various localized groups of neurons show a definite difference in resistance (or susceptibility).

3. There is a certain amount of difference in susceptibility even within cells of the same group, but it is of lesser degree than the group differences. Small cells seem to be markedly more susceptible than large ones.

4. The cerebral cortex is most susceptible (although the olfactory area, with the exception of one region of the cornu ammonis, is markedly resistant). It is followed by the Purkinje cells of the cerebellum and certain correlation and sensory cell groups. The motor cells of the midbrain, pons and medulla show the strongest degree of resistance.

5. There appears to be a localization of injury to nuclear groups. It is suggested that these groups are not only anatomical units, but also metabolic ones.

It is pointed out that the extreme sensitivity of the brain to ischemia and anemia is of great clinical importance and that lesions observed clinically are often similar to those reported here. 24 figures.

#### A COMPARISON OF THE EFFECT OF 7% CARBON DIOXIDE WITH 93% OXYGEN, AND PURE OXYGEN, ON GOATS AND DOGS, ACUTELY ASPHYXIATED WITH CARBON MONOXIDE

K. K. VINING, JR., J. L. WHITTENBERGER AND A. C. WOLLACK

Federation Proc., 5: 209, 1946

A mixture of 7 per cent carbon dioxide and 93 per cent oxygen was used for 10 minutes as inhalation therapy on goats and dogs sustaining an arterial saturation of 60 to 80 per cent carbon monoxide. The rate of elimination of carbon monox-

ide, the effect on blood carbon dioxide levels, on blood pressure and on minute volume of respiration, were compared with similar data on 2 groups of goats and dogs similarly asphyxiated, but treated with pure oxygen or room air.

The animals treated with 7 per cent carbon dioxide in 93 per cent oxygen eliminated an average of 10 per cent more carbon monoxide than those treated with pure oxygen. The arterial blood pressure fell in all animals and was between 55 and 100 millimeters of mercury in about one-third of the animals. The pressure rose to normal in animals treated with the carbon dioxide-oxygen mixture, rose an average of 60 per cent of the acute fall in animals treated with pure oxygen, but continued to fall or remained low in the air treated group.

Minute volume respiration increased an average of 110 percent when the carbon dioxide-oxygen mixture was breathed. There was no increase when pure oxygen or room air was breathed.

During gassing, the arterial carbon dioxide contents decreased to an average 63 per cent of the original values. In those animals treated with the carbon dioxide-oxygen mixture, the level rose to an average of about 78 per cent of the original values, but remained low or continued to fall in those animals treated with pure oxygen or room air.

There was no evidence of respiratory or circulatory depression during the period of inhalation of 7 per cent carbon dioxide in 93 per cent oxygen, or following its use.

## THE FETAL CIRCULATION IS IDENTICAL WITH THE VENOUS CIRCULATION OF THE ADULT MALE AND FEMALE

LOUIS DROSIN

Am. J. Surg., 71: 646-651, 1946

The author finds it advisable to show that the fetal circulation during the first 3 to 3½ months is arterial or hyperarterial and that it is venous thereafter; that its circulatory apparatus is constituted with appurtenances to carry on a large scale venous circulation; and that near birth and at birth the circulation changes to arterial and venous variety, and that the venous circulation is identical with the venous circulation of the adult male and female.

That stage of fetal existence from conception to 3 or 3½ months is designated as the proliferative stage, before active life has set in, and during it the fetus is supplied with arterial blood. From the end of the proliferative stage until near birth and at birth, the fetal circulation is venous. Because the fetal body and consequently the fetal heart is atonic or hypotonic, and not subject to the vasoconstrictor and vasodilator influence or but slightly so, it does not pump blood but blood is pumped through it. The fetal circulation is initiated, stimulated and carried on by the maternal heart and relayed by way of the uterine contractions, uterine muscle activity, placental circulation and fetal heart. The uterus possesses an undulating mechanism which climaxes into uterine contraction,

receding again to undulations. The fetal veins and heart permit reflux of blood without incidence of murmurs.

The estimates of oxygen in the fetal blood are made after delivery when it has acquired additional oxygen through the uterine contractions of labor, atmospheric pressure and actual respiration. However, all fetuses delivered as miscarriages and, as Eastman's studies show, all fetuses during cesarean section before the membranes are ruptured, are cyanotic, which again shows that the fetal circulation, before it is in contact with atmosphere, is strongly venous. During labor, there develops a combined arterial and venous circulation to counteract the increased content of carbon dioxide. The author points out the source of retroplacental clots and free blood and the cause for the various states of oxygenation.

The fetal circulation is largely stimulated by a tendency to vacuum formation and its prevention. In adults the vacuum circulatory mechanism is supplemented by the expiratory tendency to vacuum formation and its prevention, and they both form an equation; one is to the other as the other is to the one. The independent circulation in the newborn is initiated by the stoppage of the placental circulation causing an urge in the fetus to seek its own oxygen supply. It finds this urge gratified by atmospheric pressure forcing air into the larynx and through the skin when the fetal body is released from the pressure and compression of labor; and together with the change of temperature (higher or lower) they all culminate into the system of respiration.

The fetal circulation with its rate about twice that of the mother's is identical with the venous circulation of the adult male and female. The adult heart beats are about one-half the rate of the venous circulation due to the rhythmic action of respiration, increased blood pressure, absence of fetal heart appurtenances, acquisition of muscular size and tonicity of the same, together with the vasoconstrictor and dilator system of control.

While the venous circulation is of a low pitch, the fetal heart sounds, identical with it, are of a more intense nature and of higher pitch as a result of the additional sounds caused by systole and diastole. The extension-rotation reaction of the fetus to atmospheric pressure is, as a rule, the first visible evidence of extrauterine life. It is also the first instance of extrauterine vacuum presence and the inspiratory tendency to counteract it.

### CAUSES OF PREMATURITY; INFLUENCE OF UTERINE BLEEDING ON THE INCIDENCE OF PREMATURITY

ETSELLE W. BROWN, R. A. LYON AND NINA A. ANDERSON

*Am. J. Dis. Child.*, 71: 482-491, 1946

The present study is based on the records of 13,329 mothers and infants. Mothers who had no abnormality of pregnancy except bleeding and those who had entirely normal pregnancies have been placed in separate categories and

comparison of prematurity rates among the offspring of these different groups has been made to obtain information regarding the influence of bleeding on the incidence of prematurity.

The occurrence of uterine bleeding during pregnancy was accompanied by a decided increase in the incidence of prematurity. Among the offspring of white women who had only the mildest form of bleeding the rate of prematurity was 14 per cent; among the offspring of those with placenta previa the rate was 30 per cent; and among the offspring of those with premature separation of the placenta the rate was 53 per cent. These rates were in distinct contrast to that of 7 per cent, the rate of prematurity in the offspring of mothers who had no symptoms of bleeding throughout pregnancy. In the Negro women uterine bleeding during pregnancy occurred less often than in the white women, but the incidence of prematurity was approximately the same among the offspring of the 2 groups. This was especially true when prematurity among Negro infants was restricted to those whose birth weight was less than 5 pounds, 3 ounces (2350 gm.).

Among the white women whose only abnormality during pregnancy was uterine bleeding, the incidence of prematurity in the offspring of those who had mild bleeding was 15 per cent; among those with placenta previa it was 29 percent; and among those with premature separation of the placenta it was 55 per cent. The incidence of prematurity among the offspring of women who had no abnormalities during pregnancy was 5 per cent. The rates were approximately the same in the Negro race.

The occurrence of other illnesses, such as toxemia of pregnancy or syphilis, together with bleeding did not increase the incidence of prematurity above the levels associated with bleeding alone. The authors conclude that the conditions responsible for uterine bleeding during pregnancy have a more decided influence on the incidence of prematurity than any of the other illnesses commonly associated with pregnancy.

## FACIAL CHARACTERISTICS OF INFANTS WITH BILATERAL RENAL AGENESIS

EDITH L. POTTER

*Am. J. Obst. & Gynec.*, 51: 885-888, 1946

A condition of the newborn having a characteristic facial appearance which has not been previously recognized is complete renal agenesis. The author has now observed 15 such cases. In examining the earlier cases, the fact that the facial change was specific to renal agenesis was not recognized; it was considered that it might possibly constitute an unusual form of mongolism. However, further study has demonstrated that the appearance differs markedly from that found in association with mongolism. In 2 recent instances the absence of the kidneys has been correctly prognosticated prior to examination of the interior of the body, because of the facial appearance.

This facial expression has not been observed in association with death from any other cause. The most striking feature consists of an increase in width between the eyes and the presence of an unusually prominent fold arising at the inner canthus of each eye. The fold sweeps downward and laterally to form a wide semicircle under the inferior medial aspect of each orbital space. Other changes which, when combined with the appearance of the eyes, give the infant the look of an extreme premature senility are a flattening and slight broadening of the nose, an unusually receding chin and large, low-set ears which have proportionately little cartilage.

The outlook for infants with renal agenesis is hopeless, regardless of whether the condition is diagnosed prior to necropsy. However, the recognition of this facial expression may aid in arriving at a diagnosis in at least an occasional infant. 4 figures.

## THE SECULAR TREND IN THE STILLBIRTH-RATE

IAN SUTHERLAND

Lancet, 1: 756, 1946

The author states that in England and Wales there are 20,000 stillbirths a year, a figure equivalent to 65 per cent of the total infant deaths under one year of age. This large loss of life at birth is particularly serious in view of the declining birth-rate.

An examination of the figures published by the Registrar-General for the 17 years from 1928 to 1944 shows a wide variation in the mean stillbirth-rate between different areas. The data are divided into 4 groups: London administrative county, other English administrative counties, English and Welsh county boroughs, and the Welsh administrative counties. It is seen that the relative positions in the experiences of these 4 types of area are maintained throughout the 17-year period. The stillbirth-rate does not appear to increase with density of population. In recent years the inequalities between the groups have become less marked.

The trend is similar in each group and consists of an initial slight rise until 1932 or 1933, followed by an increasingly rapid decline. It is especially noteworthy that it should accelerate under war conditions, when so many factors would appear to militate against it. In the Welsh counties the decrease between 1938 and 1944 is 33 per cent of the pre-war figure and in London, despite the bombing, the corresponding decrease is 18 per cent. Little is known of the causes of stillbirth; therefore, the reasons for the decline are obscure and require further investigation.

## PLASMA IRON IN NEW-BORN BABIES

D. A. K. BLACK AND M. G. P. STOKER

Nature, London, 157: 658, 1946

In the present investigation, venous blood from the mother and blood from the placental end of the newly cut umbilical cord were used and plasma iron was estimated by the thiocyanate method. The results obtained were from 10 full-term infants and their mothers, of whom 5 were anemic. In 8 of the 10 cases, the fetal serum iron was higher than the maternal; of the 2 exceptions in one the value for the maternal serum iron was very high and contamination may have occurred, while in the other the infant had hydrocephalus and spina bifida and may have been otherwise abnormal.

The explanation for the higher fetal serum iron does not lie in a different serum protein level, for maternal and fetal serum proteins were estimated in 6 of the 10 cases and showed no significant difference. There is some evidence that the "turnover" of blood in the fetus approaching term is rapid, and the slight increase in serum iron might be of the same nature as that found in some cases of hemolytic anemia.

## OPERATIVE OBSTETRICS

### A TEN-YEAR SURVEY OF CESAREAN SECTION AT THE NEW HAVEN HOSPITAL

H. THOMS AND M. S. GODFRIED

*Am. J. Obst. & Gynec.*, 51:880-884, 1946

The present study includes 633 consecutive instances of cesarean section performed at the New Haven Hospital during the 10-year period from 1935 to 1944, inclusive. In the ward series for this period there were 190 cesarean sections in 6238 deliveries, an incidence of 3.2 per cent. In the private series there were 443 operations in 4580 deliveries, an incidence of 9.6 per cent.

In the entire series there were 2 deaths, one from hemorrhage and shock following a Latzki type section, and the other as a result of incompatible blood transfusions (this occurred when the laboratory determination of the Rh factor was not being done routinely). Thus, there was a gross maternal mortality of 0.31 per cent, and a corrected mortality, in so far as the operation itself was concerned, of 0.15 per cent.

In the ward series, 29 per cent of patients showed a temperature rise to 100.4 degrees F. or more some time during two 24-hour periods while in the hospital. The corresponding figure among the private patients was 19 per cent.

A study of the types of anesthesia used for both series throughout the 10-year period shows an interesting shift from ethylene to cyclopropane and subsequently to pentothal.

Chief among indications for section in the entire series was disproportion which accounted for 34.2 per cent of the operations. Second was previous section, and next in order was toxemia of pregnancy, followed by premature separation of the placenta and placenta previa. In regard to the chief indication for section; i. e., disproportion, the authors state that roentgen pelvimetry has been available and used by both groups of patients. In the ward service, this procedure has been part of the routine prenatal examination of every primigravid patient for almost the entire 10-year period. While this may increase the incidence of cesarean section, it is also clear that it prevents the performance of the operation where disproportion is suspected but does not actually exist, and permits necessary section to be performed at the proper time, rather than too late.

In respect to the relatively low corrected maternal mortality, the contributing factors are considered to be the competence of the operators, and the fact that in New Haven, during 1944, 98 per cent of all deliveries were in hospitals; the latter fact indicates that the incidence of prenatal examinations is relatively high. This and the high rate of hospitalization limit the deaths from puerperal causes.

## SOCIAL AND LEGAL ASPECTS

### MONOZYGOTIC AND DIZYGOTIC TWIN BIRTH FREQUENCIES IN THE U. S. POPULATION

H. H. STRANDSKOV AND E. W. EDELEN

Anat. Rec., 94: 404, 1946

It is generally stated in textbooks and other publications that about one-fourth of all U. S. twin births are monozygotic or of the one-egg type. An analysis of 365,680 U. S. sets gives an estimate of 33.43 per cent. Racial differences are found. In the U. S. "white" population the estimated percentage of monozygotic twin births among all "white" twin births is 34.17. In the "colored" population it is 28.89. This racial difference is statistically significant.

Although the "colored" population has a significantly lower proportion of monozygotic births among all twin births it actually has a higher percentage of both monozygotic and dizygotic births among all births. The respective estimated percentages in the "colored" population are 0.409 and 1.006. In the "white" population they are 0.386 and 0.743 per cent. Both of these racial differences are statistically significant.

### A COMPARISON OF STILLBIRTH PERCENTAGES AMONG SINGLE AND PLURAL BIRTHS IN THE TOTAL, THE "WHITE" AND THE "COLORED" U. S. POPULATIONS

H. H. STRANDSKOV AND DORIS ONDINA

Anat. Rec., 94: 423, 1946

Stillbirth percentages in the total U. S. population for the 15-year interval considered (1922 to 1936 inclusive) increase from 3.5 among single births, to 7.5 among twins, to 14.3 among triplets, and to 19.9 among quadruplets. All the differences are statistically significant. The stillbirth percentage among males, in each of these types of birth, is significantly higher than that among females.

Racial differences are found. For the "white" and the "colored" U. S. populations, the respective stillbirth percentages are 3.1 and 6.5 among single births, 6.6 and 13.3 among twins, 12.2 and 23.3 among triplets, and 19.4 and 21.7 among quadruplets. Most of these differences are statistically significant. For each type of birth in each population the stillbirth percentage among males is significantly higher than that among females.

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# Maternal Mortality Reports

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*(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.*

*Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)*

## CASE NO. 17

The patient was a twenty-three year old white multipara who was admitted to the hospital on November 26 at 7:15 P. M. Her serologic test for syphilis was negative and the estimated date of confinement was November 7.

The patient's past history is non-contributory. She had had a total of eight pregnancies within the past nine years, one of which terminated spontaneously at twelve weeks and the remainder went to full term. She was delivered of her last child about one year ago and during that pregnancy there was persistent glycosuria for which she was admitted to the hospital for study. Case investigation revealed no underlying pathology. Her largest baby weighed nine pounds.

The present pregnancy was normal throughout with the exception of slight occasional heartburn. According to the patient's statement the membranes had ruptured two hours prior to admission to the hospital and she had not been seen by a physician throughout the course of her pregnancy. Her physical examination upon admission revealed a well developed, well nourished white female who appeared to be much older than the stated age. She answered questions unintelligently and had a rather vacant staring facial expression. The heart and lungs were normal, the uterus measured 35 cm. above the symphysis. The fetus lay in a R.O.A. position and the fetal heart tones were good. The child was estimated to weigh about six and one-half pounds. The external pelvic measurements were normal. Rectal examination showed the cervix to be uneffaced and about 1 cm. dilated with the presenting part about 3 cms. above the spines. The blood pressure was 110/50 and the urine showed a two plus albumen. There was some bloody show present but the patient did not complain of any discomfort and no uterine contractions could be felt. She was observed overnight in the hospital but failed to go into labor. The next morning a sterile pelvic examination was done and the cervix was found to be soft and about 4 cm. dilated with the presenting part 1 cm. above the spines. At this time internal pelvic measurements were found to be ample. Clear amniotic fluid escaped from the uterus during the examination. An attempt was made to induce labor with the administration of castor oil, an enema and increasing doses of pitocin of which she received a total of 10 mm., the last being given at 2:40 P. M. Her blood pressure was 108/50 at 3 P. M., the pulse rate 100 per minute and respirations 20 per minute. Uterine contractions occurred every five minutes, lasting from 20 to 25 seconds and rectal examination disclosed the cervix to be 5 cms. dilated and the presenting part at the level of the spines.

At 4 P. M. her temperature had risen to 101°F., the blood pressure was 108/60 and rectal examination showed no change. At 6 P. M. the blood pressure was 100/70, pulse rate 88,

respirations 24 and contractions were occurring every 3 to 5 minutes, lasting 35 to 40 seconds. There was no change in the cervical dilation.

At 10 P. M. the blood pressure was 110/80, pulse 104 and respirations 40 per minute. The patient appeared to be apprehensive and examination still showed no advance in the progress of the labor.

On November 28 at 1 A. M. the patient complained of some nausea and appeared to be quite tired. At 2 A. M. the contractions of the uterus which had been somewhat irregular for the past several hours practically ceased. The blood pressure at this time was 110/78 and the fetal heart tones 160 per minute. From 4 A. M. to 10:30 A. M. the pulse ranged from 92 to 112 per minute and the temperature from 99.8°F to 100.8°F. The respirations varied between 26 and 32 per minute. There were a few irregular and poor contractions and a moderate dark brown vaginal discharge. The fetal heart tones became much more rapid and varied from 160 to 192 per minute. At 10:30 A. M. the patient was given 40 mgm. of stilbestrol in the hopes that this drug would sensitize the uterus for a second induction of labor if that became necessary. At this time she was apparently not in active labor.

At 5 P. M. she complained of some pain around the rectum for which she was given a grain of codein hypodermically and an opium suppository. She supposedly spent a quiet night, uterine contractions being entirely absent. On the following morning at 9:30 A. M. the patient was noticed to be apprehensive and her face was pinched and her eyes appeared sunken. The pulse was rapid and thready. She stated that approximately one half hour before she had turned on her side and felt a severe pain in the left lower quadrant. Palpation revealed tenderness in the left lower quadrant but no rigidity of the abdominal muscles was made out. The blood pressure at this time was 88/68. She was distended above the pubis and what was thought to be the outline of the urinary bladder was observed extending almost to the umbilicus. Catheterization was ordered and at this time the presenting part was observed at the vulva. No fetal heart tones had been heard since 10 A. M. of the preceding day. The patient, however, stated definitely that she felt fetal movements. She was taken to the delivery room where 500 cc. of plasma and  $\frac{1}{4}$  of a grain of morphine was given. Catheterization gave only 75 cc. of bloody urine. Under gas and oxygen anesthesia a hydrocephalic stillborn fetus with spinabifida, weighing 8 lbs., 2 oz., was delivered with the assistance of low forceps without difficulty. In an attempt to minimize the blood loss ergotrate was given intravenously as the anterior shoulder was being delivered. Some difficulty was encountered with the third stage of labor and after twenty minutes the placenta was extracted from the uterus manually. At this time 1,000 cc. of 5% glucose was started, the patient's blood pressure was 95/60. Exploration of the uterus revealed the uterine cavity to be intact. The cervix was lacerated deeply over  $\frac{3}{4}$  of its circumference in such a manner that it amounted to a partial amputation involving the anterior lip and part of the posterior lip. The vagina was packed with gauze moistened in saline and the blood loss was estimated at 400 cc. The patient's pulse was rapid and weak but the uterus remained firm and contracted. 350 cc. of whole blood was given since this was the only amount of her type available. The pulse was not perceptible and the breathing became rapid. In spite of stimulants and oxygen inhalations the patient became more and more shocked and at 8 P. M. the temperature rose to 104.3°F. Plasma and more glucose were given but her course continued downhill and at 8:15 A. M., about 20 hours after delivery, respirations ceased.

The vaginal packing was removed postmortem and found to be stained pale pink. There was no free blood or clots present. A gloved hand was inserted into the vagina and no lacerations of the birth canal were found. A postmortem examination was refused.

*Discussion:* The death certificate submitted by the physician in charge of this case gave "shock—undertermined origin" as the cause of death.

From hindsight it is reasonably clear that this patient must have had an unrecognized and untreated rupture of the uterus in spite of the repeated in-

sistence that there was no tear through the body of the uterus. The cessation of pains followed by the dark vaginal discharge, the bloody urine obtained on catheterization after a prolonged labor in which the patient did not receive adequate support all seem to add up to a ruptured uterus, particularly in a multipara, whose chances of suffering this accident were increased after having had eight pregnancies in the past nine years. The committee voted this death to be preventable.

#### CASE NO. 18

This patient was a twenty year old colored primigravida who was admitted to the hospital on January 11 because of the onset of labor.

Her family history was non-contributory. The patient had been treated for syphilis for the past year. Her last menstrual period was March 30 and the estimated date of her confinement was January 6. Her pains began at midnight on January 10 and on admission the heart and lungs were negative. Blood pressure 120/74. The fundus of the uterus was 30 cm. above the symphysis, the fetus lay in an R.O.A. position, the presenting part was floating and the fetal heart was heard in the R.L.Q. She was thought to be at term with a fetus weighing between eight and nine pounds. The external measurements of the pelvis were spines, 22 cms, crests, 26 cm., intertrochanteric 31 cm., Baudelocque, 21.5 cm. and T.I. 8.5 cm. Rectal examination showed the cervix to be thick, 2 cm. dilated and on admission the pains were about three minutes apart but quite weak in character.

The uterine contractions grew milder throughout the day following admission and at 12:50 A. M., January 12, she was given three grains of seconal; at 4:00 P. M. the cervix was 3 to 4 cm. dilated and the head was 2 cm. above the spines and it was not until midnight on January 12 that the head was level with the spines. The patient's pulse rate did not exceed 88 per minute at any time during all of this period but the uterine contractions were never particularly good. At 11:00 A. M. the cervix was 4 to 5 cm. dilated and the head 2 cm. below the spines. At 12:05 A. M. on January 13 the membranes ruptured and the patient was given 100 mgms. Demoral and  $\frac{1}{2}$  gr. of Scopolamine. At this time the fetal heart was faint and from 6:30 P. M. on of this day it was no longer heard. At this time the cervix was only 5 to 6 cm. dilated. The patient's pulse rate was now beginning to be accelerated and on January 13 it was counted at 120 beats per minute on several different occasions. At 8:00 P. M. of this day the temperature had risen to 100°F. At 10:15 A. M. on the following day only a rim of the cervix was left but the pulse rate was 140 at this time. The patient was given 1,000 cubic centimeters of five per cent glucose and 500 cubic centimeters of saline solution intravenously. An x-ray taken on this day gave the following impression: "normal pelvis, large baby, right-occipito-posterior, head at spines, no definite overlapping of skull bones". A sterile pelvic examination was made at 4:00 P. M. on January 14 and it was found that the presenting part was at the spines, that the head was not well flexed. The cervix was 8 centimeters dilated and at the time of this examination there was found a thick, foul smelling vaginal discharge.

A fetal scalp clamp was applied at this time because the pains were poor. On catheterization no urine was obtained because of the difficulty of inserting the catheter into the bladder. Two hours later catheterization was again attempted but was again unsuccessful. The patient was now started on 25,000 units of penicillin every three hours even though her highest temperature on January 14 was 99.6°F. At 12:30 A. M. on January 15 the patient was fully dilated and the head 3 cm. below the spines and it was not until 7:30 A. M. that consultation was requested which resulted in the advice to attempt to deliver the patient with forceps but if any difficulty was encountered to do a craniotomy. The patient was prepared for delivery and 1 ounce of highly colored urine was obtained on catheterization. Forceps were applied but upon traction it was not possible to deliver the fetus. Craniotomy was then done an 8 lb. 7 oz. infant delivered at 8:50 A. M. on January 15. A medio-

lateral episiotomy was done. The third stage was fifteen minutes in duration and presented no abnormalities. The episiotomy and vaginal lacerations were repaired. The entire operative procedure was done under nitrous oxide, oxygen and ether anesthesia. The patient was returned to the ward with her uterus well contracted but still not awake from her anesthesia. She never aroused from the anesthesia and died at 10:15 A. M. on January 15.

Autopsy revealed lobular pneumonia, acute suppurative endometritis, diffuse infiltration with areas of necrosis in the uterine wall, hemorrhage and focal necrosis in both kidneys, focal hemorrhages and many polymorphs in the spleen.

*Discussion:* It is rather interesting that the certificate of death in this case showed the single word "toxemia" as the sole cause of death. A word here would not be amiss concerning the importance of properly giving the true cause of death in the medical certification on the certificate. It is obvious that this patient died of a combination of three causes, namely: intrapartum infection, shock due to operative trauma and probably hemorrhage. This patient, who died one hour and twenty-five minutes after delivery, might have been helped by a transfusion between the time of her delivery and the time of her death. Certainly there was inadequate support and rest during the four days in which she was in labor. The prolonged labor, the intrapartum infection and the terminal pneumonia do not make an unfamiliar pattern. She was particularly vulnerable to blood loss and trauma. The anuria which was probably due to dehydration made her even more vulnerable. The attempted forceps and the added craniotomy augmented the shock, particularly in this situation where we are dealing with a patient in poor shape. This death was judged to be a preventable one.

#### CASE NO. 19

The patient was a 17 year old colored primipara who was admitted to the hospital on July 27 with a diagnosis of acute pre-eclampsia. The family history and personal history were noncontributory. She was first seen on February 2, at that time her general physical examination was negative and the last menstrual period was November 5 with an estimated date of confinement on August 12. The patient's blood pressure was 120/70, her weight 110 pounds and the external pelvic measurements slightly below normal. She was followed regularly in the prenatal clinic and her blood pressure remained normal and her weight gain was not excessive until her visit on July 27, at which time the blood pressure which had been 110/78 the week previous was found to be 160/130. The urine revealed four plus albumin and both ankles were markedly edematous. She was immediately hospitalized.

Upon arrival at the hospital at 2:30 P. M. the temperature, pulse and respirations were normal and the blood pressure was 160/130. With the exception of the hypertension and the marked ankle edema and the albuminuria, the patient presented no signs or symptoms worthy of note. She was put to bed on a salt poor diet and was given 50 mgm. of thiamine chloride. Roentgenpelvimetry showed the antero-posterior diameter of the pelvic inlet to be 10.5 cm.; the right oblique diameter to be 10.5 cm., the left oblique diameter to be 11.0 cm. and the transverse diameter to be 11.3 cm.

At 7 P. M. she was given 250 cubic centimeters of 25% glucose and 100 cubic centimeters of 5% glucose intravenously. The blood pressure slowly fell and by midnight it was 140/80 but it soon rose again so that at 4 A. M. on July 28 it was 160/110. At 8 A. M. the thiamine chloride was repeated and an order left for its administration every four hours. At 5:30 P. M. she was given 250 cubic centimeters of 25% glucose and 4 cubic centimeters of 50% magnesium sulphate. During all this time her blood pressure remained elevated going as high as 174/110 on one occasion. A specimen of urine examined at this time was negative

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## FUNCTIONAL UTERINE BLEEDING

### *A Summarizing Review*

BY EMIL NOVAK, M.D.

*Baltimore, Md.*

One of the most frequent and, under certain conditions, one of the most distressing problems in gynecological practice is that of functional uterine bleeding. While we have considerable knowledge as to the mechanism involved in at least one large group of cases, we know almost nothing as to the etiology of others. What we do know concerning the causation of functional bleeding pertains almost entirely to endocrine factors, but there are other cogs in the complicated machinery of the menstrual function which may conceivably undergo aberrations of one sort or another—the musculature of the uterus, the vascular mechanism of the endometrium, and the vasomotor nerve apparatus. But we can only speculate as to the possible role of such factors in bringing about quantitative abnormalities of the menstrual flow.

Even in the type of bleeding which we flatter ourselves that we do know something about, the so-called metropathia hemorrhagica, our methods of treatment are still rather superficial and, in the main, unsatisfactory, except in those cases in which the patient's proximity to the menopause justifies resort to absolute abolition of the menstrual function. The present paper can make no pretense to being an exhaustive review of the really vast literature of the subject which has accumulated, especially during the past thirty or forty years. It is to be taken simply as a purely personal summarizing appraisal of the present status of the question, with the extenuation that it is based on a rather large and long clinical experience with functional bleeding, and a reasonable familiarity with the literature. The appended bibliography includes references to a good many of the more important older contributions to the subject, and a fairly complete listing of articles published during the past ten years. Most of the latter, unfortunately, have added little to our knowledge of either the etiology or the treatment of functional bleeding, but a review of this sort may serve at least to bring us up to date as to prevailing concepts. A preliminary historical sketch will serve as a background for present day ideas and practices.

### HISTORICAL

The term functional bleeding did not come into general use until well after it had been demonstrated that the ovary is an organ of internal secretion, and this

was not until the closing years of the preceding century. Before this the rather meaningless designation of idiopathic bleeding was the one most frequently applied. The earlier concept of the role of the ovary in functional bleeding was very simple, hyperfunction being blamed for the bleeding, just as menstrual scantiness or absence was explained by deficiency of the then rather mythical internal secretion of the ovary. Moreover, many cases which are now interpreted as functional were explained by anatomic factors of one sort or another.

As far back as 1860 Scanzoni, in his work "Ueber die Chronische Metritis", argued that chronic metritis is the most common of female diseases, the myometrium being often diseased even when the endometrium is normal. He explained the bleeding as due to an abnormal brittleness of the arteries. Many years later, and after the ovary had been shown to have an endocrine function, Theilhaber (1910) devoted numerous papers to the propagation of his theory of "insufficiencia uteri", the factor of defective contractility of the mesometrium being ascribed the chief role in the production of abnormal bleeding. He used the term mesometrium in preference to myometrium in order to embrace in his concept the connective tissue as well as the musculature of the uterus. Other investigators, like Anspach (1909) considered certain types of uterine bleeding ("metrorrhagia myopathica") to be due to failure of the normal increase of elastic tissue which takes place toward the end of menstrual life, or of the normal obliterative changes in the blood vessels, or an excessive hypertrophy of connective tissue, making firm contraction of the uterus impossible, and thus giving rise to menorrhagia or metrorrhagia.

A somewhat similar view, with emphasis on the increased elastic tissue in the blood vessel walls, was urged by Pankow (1909). Incidentally this writer employed the term metropathia hemorrhagica, later applied by Schröder to an important variety of functional bleeding, and this term is still in common use. Many other writers, like Reinecke (1897), Slocum (1908) and Findley (1905), attached great importance to uterine arteriosclerosis as a cause of bleeding, and the term apoplexia uteri, said to have been first used by Cruveilhier, began to creep into the literature. There is no doubt that the group of cases for which these various explanations were offered embraced chiefly those now considered as endocrinopathies, and it is quite possible that we have gone too far to the other extreme in emphasizing endocrine factors, as will be touched upon later.

### PRESENT DAY CONCEPTS OF MECHANISM

While nearly a third of a century elapsed between the discovery of the endocrine function of the ovary and the isolation of either of the two ovarian principles, histological studies had made it quite certain, long before the latter event, that two separate hormones must be present, one emanating from the follicle and one from the ovary. Such correlative studies, moreover, led Schröder (1915) to evolve for the first time a working concept of the mechanism involved in the most frequent variety of functional bleeding, that which he designated as metropathia hemorrhagica. I am told by some of my South American confrères that the designation of Brennecke-Schröder disorder is often applied to this

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#### HISTORICAL

The term functional bleeding did not come into general use until well after it had been demonstrated that the ovary is an organ of internal secretion, and this

interrelationship, and this knowledge has been applied not only to the explanation of the normal menstrual cycle, but also to that of functional bleeding. While there is some evidence to indicate that small doses of estrogen may be pituitary stimulants, the weight of evidence still supports the view that when the level of estrogen reaches a certain point, which evidently differs widely in different species and different individuals of any one species, there occurs a reverse inhibition of the follicle-stimulating pituitary hormone, with resulting inhibition of follicle growth in the ovary, and thereby a drop in estrogen production.

To illustrate with the classical picture of functional bleeding associated with hyperplasia of the endometrium, this abrupt drop in estrogen precipitates a bleeding phase. This is in conformity with what is apparently a general law, that so long as the endometrium is receiving a steady supply of its supporting hormone or hormones, either estrogen alone or, in the case of normal menstruation, estrogen supplemented by progesterone, it does not bleed. But when this endocrine support is rather abruptly cut off, bleeding follows after an interval of a varying number of days, depending chiefly on the duration and dosage of the estrogen influence.

This, in any event, appears to be the generally accepted view as to the alteration of bleeding and non-bleeding phases, but it quite surely does not tell the whole story. Certainly the hormone effects cannot be expressed in any simple mathematical terms, because there must be wide variations in the degree of sensitivity or refractoriness of individual ovaries to the gonadotrophic hormones, and of individual endometria to the ovarian hormones.

There is, furthermore, no parallelism between the growth propensities and the bleeding propensities of the endometrium. In some cases the growth effect may be very striking, as expressed by extreme degrees of hyperplasia, and yet with little or no bleeding. In other cases the growth effect may be very slight, and the endometrium may even be atrophic, and still the patient may have profuse bleeding. This separateness of the growth and the bleeding reactions in the endometrium, to which various authors have called attention (Novak, Rock) is expressed in the common statement, undoubtedly true, that abnormal bleeding can occur from an endometrium of any histological type.

This latter statement includes not only wide variations in the degree of estrogen effect upon the endometrium, but can be extended also to the fairly numerous cases of functional bleeding in which the endometrium shows definite and sometimes very pronounced evidence of secretory reaction. In such cases, by all our accepted criteria, ovulation is occurring, in contrast with the larger group of metropathia hemorrhagica cases, in which ovulation is obviously in abeyance. In other words, the latter represent aberrations of anovulatory cycles, while those with secretory endometria represent disorders of the far more common ovulatory cycles.

The fact that the relatively uncommon anovulatory cycle is proportionately far more often thrown out of gear, so to speak, would seem to suggest that it is a more primitive and less stable type. Again, it is in the inaugural years of menstrual life, and, even more often, in the closing years of the function, that we

condition in the South American countries. It may be recalled that as far back as 1882 Brennecke had described the so-called endometritis ovarialis, some of his cases being evidently those which we now designate as hyperplasia of the endometrium and which he correctly suggested might be due to the influence of the ovary. This, however, was long before we knew the ovary to have a hormone function, and it is Schröder whose thorough studies gave us our present concept of metropathia hemorrhagica, through the medium of his classical contribution on "Anatomische Studien zur normalen und pathologischen Physiologie des Menstruationszyklus." (1915).

By the correlated study of the endometrium and the ovaries in a large number of cases, he was able to demonstrate that the disorder is due to a failure of ovulation, with abnormally long persistence of the follicle, and with, of course, absence of the corpus luteum. It was later shown (Meyer) that instead of a single persisting follicle a considerable group of partially mature follicles might thus persist. Translated into endocrine parlance, there is in such cases an abnormally persistent influence on the endometrium of the follicular estrogen, producing the exaggerated growth picture which we call hyperplasia. Nor, since progesterone is absent, is there any evidence of secretory effect upon the endometrium. I once asked Schröder, when he visited me in Baltimore, how he was able to collect such a large number of uteri and ovaries for this study, since functional bleeding so rarely calls for radical operations. He told me that most of it was accumulated when he was an assistant in Rostock under Sarwey, whose treatment of such cases was far more radical than that generally employed then or now.

Since this fundamental work of Schröder two important additions have been made to our knowledge of the mechanism of metropathia hemorrhagica. Both of the ovarian hormones have been isolated, so that it has been possible to attack the problem experimentally. By persistent dosage with adequate, but not necessarily, very large amounts of estrogen it has been possible to produce typical hyperplasia in previously castrated animals. Secondly, since the publication of Schröder's paper in 1915 we have learned a great deal as to the domination of ovarian function by the anterior hypophysis, and as to the dual hormonal nature of this control, through the follicle stimulating and luteinizing gonodotrophic principles.

The pioneers in this work were Smith and Engle in this country, and Zondek and Aschheim in Germany. Such investigations have indicated that the metropathia hemorrhagica type of functional bleeding, and possibly others as well, are primarily of pituitary and not ovarian origin. I shall have occasion later to stress the bearing of this on the treatment of this disorder, which has been directed almost altogether to the secondary ovarian dysfunction, chiefly because we have achieved no adequate means of readjusting the underlying pituitary dysfunction. For that matter, it has not yet been possible to isolate the pituitary sex hormones, or to prepare extracts with any noteworthy effect upon human ovarian function.

However, we have learned a good deal as to the nature of the pituitary-gonadal

metrorrhagia is also very common, as is a combination of the two (menometrorrhagia). In the more severe cases the bleeding may be continuous over many weeks or months. Whether menorrhagic or metrorrhagic, the bleeding excess may be of rather mild degree, but in other cases it is so severe as to exsanguinate the patient, and it may even be fatal.

#### TREATMENT

In the first place, it is important to remember that there are many cases of the milder forms of functional bleeding in which no treatment is called for, because they correct themselves spontaneously. This is particularly true of the anovulatory bleeding so often seen at the two extremes of menstrual life. Many girls do not begin to ovulate until many months, or even several years after the menarche, and, in the same way, many women cease ovulating a considerable time, even quite a number of years, before the menopause.

Such anovulatory cycles may be associated clinically with bleeding no freer than normal menstruation or showing so little prolongation or excess that patients may not seek medical advice. If they do they can be treated expectantly. In the case of the young girl with only slight functional excess, not sufficient to produce anemia, the initiation of ovulation is likely to bring about the inauguration of entirely normal menstruation. Unfortunately there are many cases in which the bleeding during the anovulatory phase is very profuse, so that active measures of treatment, usually of endocrine nature, must be invoked.

A similar statement can be made concerning the very common premenopausal type of functional bleeding. Slight excess, with no intermenstrual bleeding, can in the absence of any demonstrable anatomic lesion often be treated expectantly, with no direful result, and with no infringement of the general dictum that abnormal bleeding at this age epoch should be viewed with suspicion.

All too often, however, the bleeding is profuse and not infrequently prolonged, and under such conditions there should be no delay. Here we find probably our greatest field for diagnostic curettage, because at this age period functional bleeding comes into diagnostic competition with other more serious lesions, such as adenocarcinoma and submucous myoma. If no gross lesion of the pelvic organs exists, and the curettage yields any type of benign proliferative endometrium, whether genuine hyperplasia or not, or if it reveals a benign secretory picture, one is justified in considering the bleeding to be of functional nature, and to treat it accordingly.

In a not inconsiderable proportion of cases the curettage in itself appears to bring about an endocrine re-adjustment, so that subsequent menstruations are normal. This is particularly true in women very close to the termination of menstrual life, and such women can often proceed for the short remainder of menstrual life with no further treatment.

Unfortunately, however, and especially where the bleeding has been free and of long duration, and where the patients are in the late thirties or early forties, the menstrual excess recurs after a variable period following the curettage. One must therefore resort to more active and more permanent measures, involving

see the highest incidence of anovulatory cycles. It is not surprising, therefore, that it is at these two epochs that we encounter the greatest frequency of functional bleeding of the metropathia hemorrhagica type. As a matter of fact, it would seem to me that a more expressive and simpler designation for this type would be *anovulatory functional bleeding*, to distinguish it from the ovulatory variety, characterized by definite evidence of continuing ovulation.

As to the mechanism of the latter type of bleeding, we are still in the dark. We can only speculate upon the possible influence of quantitative imbalances between the two ovarian hormones, just as we can in the case of primary dysmenorrhea, which is so characteristically associated with ovulatory rather than anovulatory cycles. But there are other possible factors, such as the role of the uterine musculature, or of the spiral arteriolar apparatus of the endometrium, or even of the vasomotor nerves. Nor can we exclude from consideration the differences in sensitivity or refractoriness, already alluded to, in the recipient tissues of the ovaries, pituitary and uterus to the hormone forces which are operative in the reproductive mechanism.

The thyroid is frequently mentioned in the discussion of functional bleeding, but its association appears to be important in only a small proportion. Hypothyroidism is more likely to be associated with menstrual excess than hyperthyroidism, but there are many exceptions. For example, amenorrhea is a not infrequent symptom of thyroid deficiency. On the other hand, some time ago I saw a patient who had been taking enormous doses of thyroid, 20 grains a day, with no toxic symptoms, although the hypothyroidism, on the basis of metabolism rate and blood cholesterol, was of only moderate degree. When the dosage of thyroid was cut down materially menorrhagia invariably developed. Little is known as to the nature of the relation between the thyroid and the gonads, although it is apparently a real one. Nor is there any explanation as to the paradoxical nature of this relationship, though one would suspect that the thyro-ovarian link-up is mediated through the pituitary, and the hormonal status of the latter might bring about differences in the immediate effects upon the reproductive cycle.

The fact remains, however, that in the great majority of cases of functional bleeding, there is neither clinical nor laboratory evidence of thyroid dysfunction, and that the thyroid therapy which many employ empirically is not usually of much benefit.

#### CLINICAL CHARACTERISTICS

Not much need be said in this short review as to the clinical aspects of functional bleeding, since these are familiar to all gynecologists. Its occurrence at any stage of reproductive life, but especially at its extremes, is well known, as is the fact that by far the largest number of instances, probably more than 50 per cent, are observed in the fifth decade of life, i. e. in the premenopausal epoch. While a number of statistical studies are available on this point, they yield no additional information of great value, so that they need not be discussed here. Most characterically the abnormal bleeding is of menorrhagic type, but

excess of estrogen and a lack of progesterone, which was not to be made available for a number of years.

But in the meantime the discovery of the pituitary domination of the ovary, already alluded to above, had led to intensive studies of the gonadotrophic principle in pregnancy urine. This substance, called prolan by Zondek, was found to have markedly luteinizing effects upon the ovaries of mice and other laboratory animals, so that it was at first thought that its administration in cases of functional bleeding might lead to a similar luteinization in the human ovary, with the production of progesterone and possibly the control of the bleeding. Novak and Hurd reported its employment in 58 patients, with apparently marked benefit in many. It was soon found, however, that any benefit which might come from such treatment was not due to any histologically demonstrable luteinization of the ovaries, nor has any very satisfactory explanation been presented since then. The employment of these chorionic gonadotrophic principles, however, has continued even to the present day as one of the endocrine plans of treating functional bleeding, although it has been very largely superseded by other methods of organotherapeutic attack.

With the availability of preparations of pure progesterone in the early years of the preceding decade, it was hoped that the results of treatment might be greatly improved, since it is a lack of progesterone which appears to characterize this syndrome. It cannot be said that these hopes have been fulfilled, although good results in at least a considerable proportion of cases have been reported by many writers (Allen and Heckel, Smith, Jones and Te Linde). The paper of Allen and Heckel, dealing chiefly with the treatment of functional bleeding in young girls, reports cures in roughly one third, improvement in one third, and no improvement in the remaining third, although the dosage employed was considerably larger than that in common use among practitioners, chiefly because of the expense involved to the patient. Furthermore, it is difficult to evaluate the results of treatment in patients of this age group, because of the frequency of spontaneous cure, probably dependent upon the inauguration of ovulation after a preliminary phase of anovulatory cycles.

Other authors report varying degrees of success with this plan of treatment, which is certainly one that most of us would wish to resort to in many cases, because of its simplicity, safety and convenience, especially where oral administration is used. The various preparations of anhydrohydroxy progesterone, the form in which progesterone is given orally, are undoubtedly potent, though at least 5 times the intramuscular dose is required, and the expense to the patient is not inconsiderable.

The fact that the androgenic hormones, especially in the form of testosterone propionate, appear to exert a somewhat anti-estrogenic effect rather naturally led to their employment in the treatment of a disorder believed to be due to an excessive or imbalanced estrogen effect. This plan has achieved considerable popularity, in spite of the fact that some endocrinologists are rather bitterly opposed to it as unphysiological. As a matter of fact, it is difficult in the present state of our knowledge to be sure which methods are physiological and

either abolition of the ovarian function by radiotherapy or, under certain conditions, hysterectomy. Gynecologists will differ somewhat in their opinions as to the age at which radiotherapy in sterilization dosage is justified, and the decision in border-line cases is often based on the individual circumstances of the case. There will be no division of opinion in the case of women of 45 and over, and in my own judgment the radiotherapeutic plan is usually the safer and wiser one in most women over 40. Even in the older group, however, I would select hysterectomy if there is any other indication for laparotomy, such as a ventral hernia or a recurrent appendicitis.

In the case of women in the late thirties, and in not a few of those in the very early forties, hysterectomy will appear to most gynecologists as the wiser plan. In most cases, however, one would prefer, if all simpler measures fail, and the bleeding is a serious problem, in the cases of recurrent bleeding at border-line ages, to resort to organotherapy along such lines as have been discussed above.

In the pre-endocrine days, when functional bleeding was still spoken of as "idiopathic", the chief reliance was placed upon such drugs as ergot and hydrastis, with curettage when drugs were unsuccessful, and hysterectomy if bleeding recurred after curettage. Aside from such general measures as rest and hematinics (this was before the days of transfusion), this about represented the available armamentarium of treatment. It is true that other measures were suggested from time to time, such as atmocausis, the intrauterine application of zinc chloride (Boldt, Mayo) or formalin, but, probably fortunately, these did not achieve wide vogue.

The use of radium and X-ray in the treatment of functional bleeding seems to have been an offshoot of the application of these methods in the treatment of uterine fibroids. The very first effort in this field, using X-rays, is said by Kelly and Burnam to have been made in 1903 by William James Morton, while the same authors state that radium for the same purpose was first employed in 1906 by Oudin and Verchère. To Krönig and Gauss (1912) must go the chief credit for the popularization of radiotherapy for myoma, with rapid extension to the treatment of benign uterine hemorrhages.

#### ENDOCRINE THERAPY

Before the discovery of the ovarian hormones there was a wide spread vogue for the treatment of functional bleeding by the ovarian and corpus luteum preparations then available, though we now know that they were all practically inert. After the publication of Schröder's work it was especially the corpus luteum preparations which were employed. The empirical use of thyroid preparations was also quite popular, while the posterior lobe pituitary preparations, after their introduction into obstetrical practice, were also not infrequently used for functional bleeding because of this effect upon the uterine musculature.

It was not long after the isolation of the estrogenic hormone that potent estrogenic principles became available commercially, but no one thought then to apply them to the treatment of a disorder believed to be due to a relative

excess of estrogen and a lack of progesterone, which was not to be made available for a number of years.

But in the meantime the discovery of the pituitary domination of the ovary, already alluded to above, had led to intensive studies of the gonadotrophic principle in pregnancy urine. This substance, called prolan by Zondek, was found to have markedly luteinizing effects upon the ovaries of mice and other laboratory animals, so that it was at first thought that its administration in cases of functional bleeding might lead to a similar luteinization in the human ovary, with the production of progesterone and possibly the control of the bleeding. Novak and Hurd reported its employment in 58 patients, with apparently marked benefit in many. It was soon found, however, that any benefit which might come from such treatment was not due to any histologically demonstrable luteinization of the ovaries, nor has any very satisfactory explanation been presented since then. The employment of these chorionic gonadotrophic principles, however, has continued even to the present day as one of the endocrine plans of treating functional bleeding, although it has been very largely superseded by other methods of organotherapeutic attack.

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which unphysiological. A few seem to think that the injection of the male hormone is more or less contaminating, forgetting that during the reproductive epoch the woman normally exhibits a blood curve of androgenic hormone not unlike that of estrogen. Though no definite role for this hormone in reproductive life has been demonstrated, it is not impossible that it may have one. I mention these things because I am one of those who are not horror-struck by the use of this therapeutic plan, which in my hands and that of many others, has been more frequently helpful than progesterone.

The consideration which has limited its employment more than any other is the fact that when pushed too vigorously or too long testosterone will undoubtedly bring about hirsutism and other masculinization manifestations. These, however, do not occur when the dosage is kept below 200 mg. a month, and personally I rarely employ more than 150 mg. As a matter of fact I have never seen unpleasant sequelae with such doses, nor do any seem to be reported in the literature. If they did occur even with modest doses, there would be no justification for this method of therapy. In the more moderate forms of functional bleeding in young girls I prefer to try progesterone therapy, but in older patients, and especially when progesterone has been found ineffective, I do not hesitate to employ testosterone, usually in an intramuscular dosage of 10 mg. three times a week. I have felt justified in injecting this personal appraisal, because I believe it to represent a fair and safe compromise between the extremists on either side of the question.

Until recent years, as already mentioned, the estrogens were rarely resorted to in the treatment of functional bleeding. It was generally thought, as it still is, that the bleeding phases occurred when the estrogen level dropped below a certain point which quite surely differs very widely in different individuals and different species. It seemed logical enough to believe that by raising this estrogen level the bleeding might be checked at least temporarily, and many of us for many years have at times resorted to this plan. On the other hand, with the cessation of estrogen therapy recurrence of the bleeding might be expected. Karnaky has for a good many years urged the employment of very large estrogen dosage in the control of uterine bleeding, and it is probably fair to say that many of his tenets as to dosage, and as to extension of this plan to the bleeding of myoma and the management of threatened abortion, have not won the favor of conservative gynecologists. On the other hand, he deserves the chief credit, it seems to me, for extending the employment of estrogenic therapy for functional bleeding. As in so many other fields, it often takes an extremist to work reforms, and, while it certainly has sharp limitations, the employment of estrogens now occupies a definite place in the management of functional bleeding.

It can be carried out in various ways. The simplest plan, in the case of bleeding known to be of functional nature, is to give a daily large oral dosage, ordinarily 8 to 10 mg. of diethyl-stilbestrol until the bleeding is checked, as it will often be within a very few days. If the stilbestrol, to use the common commercial designation, be then suddenly stopped, bleeding is likely to return, but if the withdrawal is gradual, lessening the dose 1 or 2 mg. a day, there is either no return, or at most only a slight bleeding. With the return of another

bleeding phase which continues more than a reasonable number of days, or is very profuse, the large doses of stilbestrol are again resumed, with later decrease as described above.

In the milder forms of functional bleeding, this simple plan will often tide the patient over until the hoped for endocrine re-adjustment occurs, as it not infrequently does. The stilbestrol in such cases exerts its hemostatic effect by correcting the low estrogen level which is apparently the immediate cause of the bleeding. Nor are the rather large doses employed in any way harmful, although a certain proportion of patients, probably 10 to 15 per cent, cannot tolerate them because of unpleasant side effects, such as nausea and vomiting. If such effects are encountered, the natural hormones may be used in correspondingly large hypodermic or oral doses, or, more often, one of the other oral estrogens may be employed, such as hexestrol, premarin, benzestrol or ethinyl estradiol (estinyl).

Such treatment, helpful as it often is, is superficial in the sense that it is directed toward the immediate ovarian dysfunction rather than to the underlying pituitary disorder, although in some cases the latter appears to right itself, whether spontaneously or as a result of the treatment. Hamblen and Smith are warm advocates of cyclic methods of treatment, employing the estrogen and progesterone, feeling that these offer a better chance of inducing a re-adjustment of pituitary function. Hamblen, after preliminary control by large doses (6 mg.) of diethyl-stilbestrol, somewhat after the plan above mentioned, keeps up the dosage for 20 days. Its withdrawal is followed by bleeding after an interval of 1 to 5 days. On the fifth day of this withdrawal bleeding 3 mg. of diethyl-stilbestrol is begun again in daily doses for 20 days, with a third cycle of stilbestrol later, somewhat according to the same plan. On the fifth day of the withdrawal bleeding following the third cycle of estrogen therapy, 3 mg. doses of stilbestrol are again started and kept up for 20 days, but during the last 10 days of this series 10 mg. of progesterone is given intramuscularly every day or 30 or 40 mg. of anhydro-hydroxy-progesterone are given orally and daily. For patients who fail to respond to this plan he suggests a trial of what he calls one-two cyclic gonadotrophin therapy, involving daily injections of 400 units of equine gonadotrophin from the 5th to the 14th days of the cycle, followed from the 15th to the 24th days by daily intramuscular injections of chorionic gonadotrophin.

It is obvious that the expense of such treatment will make it prohibitive to most patients, while the inconvenience of daily injections for long periods of time will make many feel that the remedy is worse than the disease, especially as there is no certainty of benefit. Nor does the supposed rationale of this elaborate plan appear to all of us as unimpeachable. It appears to be based on the concept that either by ovarian or gonadotrophic therapy it is possible to beat the pituitary into a sort of cyclical submission, a very uncertain hope with a sick and poorly reacting gland. It would seem just as logical to try to convert anovulatory into ovulatory cycles by the simple expedient of supplementary progesterone therapy, a rather fatuous ambition in the present state of our knowledge.

The objections expressed above to Hamblen's plan apply also to the elaborate

and expensive ritual outlined by Smith, especially in the case of women who have more or less continuous bleeding. He recommends that "10 mg. of progesterone and 1 mg. of estradiol should be injected on the first day of treatment and 10 mg. of progesterone daily for the next 4 days. The bleeding will probably be controlled by the treatment, and a fairly normal period will occur 2 to 4 days later. Counting the beginning of this period as the first day, the same course of injections is repeated beginning on the twenty-first day. This course of treatment should be given at least twice, and may be repeated again after an interval if there is any recurrence of excessive bleeding. If the bleeding is profuse the daily dosage of progesterone is increased to 50 mg., reducing the dose as the bleeding becomes less, but continuing injections for at least 5 days or longer if necessary to control the bleeding." Following this formidable and highly expensive preliminary treatment, cyclic therapy is then begun. Even if the plan were always successful, which it is not, I cannot conceive that many patients would be willing to submit to it, especially if they have to pay for all the progesterone employed. Nor do I think it any more effective than some of the plans discussed previously in this review. For that matter, in the occasional very intractable case, I would prefer to resort, if necessary, to an occasional curettage, especially as this can be so readily performed without hospitalization and with no anesthesia where the suction curettage is done, or with a light sodium pentothal anesthesia if the customary technique is employed. Almost always this is followed by at least temporary relief from the bleeding.

All the methods thus far discussed are directed largely to the ovarian manifestations of a disorder involving the pituitary, with the hope that the latter will be indirectly influenced by the ovarian therapy. A more direct pituitary approach is attempted by the employment of the various gonadotropic preparations which have been employed, such as the equine gonadotropic principle, or, as previously mentioned, the chorionic gonadotropic hormone. I do not believe that any one will maintain that, thus far, these have yielded any conspicuously good results.

The fact remains, however, that of all the numerous cases of functional bleeding encountered by every gynecologist there is only a small proportion which are so severe and so intractable that more radical measures, such as light radiotherapy in small dosage or even hysterectomy, have to be thought of.

Certainly there would be little reason to criticize the employment of light radium dosage, not exceeding a few hundred mg. hours, in the occasional patient of the younger group who has proved intractable to more conservative measures, but the plan is not without hazard, as some ovaries are singularly sensitive to even light radium dosage, and even permanent abolition of the function may ensue. Other ovaries, on the other hand, are quite resistant, so that the effect of the mild doses ordinarily considered safe is difficult to predict. Other objections have been urged, such as the possible effect of such therapy upon subsequent generations of ova, although it must be admitted that the evidence on this point is not by any means convincing. In general, however, most gynecologists will look upon radiotherapy in young women as a method not to be resorted to unless the various plans of endocrine therapy have proved ineffective.

By one method or another of those discussed, or by some combination of methods, the lot of almost all patients can be made tolerable until the hoped for endocrine re-adjustment takes place, as it does in the great majority of cases. My own plan, and I think it a wise psychological approach, is to explain to a patient the difficulties and uncertainties of our present-day methods, and the possibility that she may be in for a career of disagreeable bleeding and therapy of unpredictable length, but to encourage her by urging that sooner or later, perhaps within a few months, but perhaps not for several years, she has an excellent chance of becoming essentially normal. With such explanations the patient is likely to be cooperative in treatment, appreciating the desire of the doctor to cure her without resort to radical procedures.

I need not here elaborate on the fact that whatever method of treatment is employed for the disorder itself, general measures are not to be neglected. In the milder forms anemia may not be a problem, but in those of more severe grade it always is, so that hematinics and transfusions are often indicated. When transfusion is done, it is a great advantage, when it is practicable, to use blood from a pregnant woman because of its high gonadotropic content. This is of double value, not only making up the blood loss, but having a beneficial effect upon the bleeding.

There are still other methods of treatment of functional bleeding which I have not discussed, such as the employment of insulin, mammary extracts, prolactin, vitamin K. vitamin B. or vitamin C. but the occasional reports of good results are so uncritical and unimpressive that it does not seem worthwhile to do more than mention them.

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## ENDOCRINOLOGY

### FUNCTIONAL RELATION BETWEEN THE UTERUS AND THE CORPUS LUTEUM

J. P. CHU AND S. S. YOU

*J. Endocrinol.*, 4: 392-398, 1946

Loeb, in 1923, found that hysterectomy in the guinea-pig causes a marked prolongation of the life of the corpus luteum, and explained his results by assuming that the uterine endometrium may secrete a certain hormone-like substance which shortens the life of the corpus luteum. In the pregnant rabbit, hysterectomy during the first half of pregnancy shortens the life of the corpus luteum, and operation performed at a late stage of pregnancy initiates a precipitous decrease in size of the corpora lutea. The question whether or not the corpora lutea in pregnant and pseudopregnant conditions are regulated by the same mechanism requires further study.

In the present investigation, rabbits were divided into 7 groups. (1) Pseudopregnant rabbits were hysterectomized at various intervals after mating. (2) Hysterectomized-pseudopregnant animals were given auto-transplants of the uterus. (3) Intact pseudopregnant rabbits were given injections of estrogen. (4) Pregnant rabbits were hysterectomized at various stages of gestation. (5) Transplants of placenta were made in hysterectomized-pregnant animals. (6) Extirpation of the placenta was performed in pregnant rabbits leaving the uterus intact. (7) Pregnant rabbits were injected with estrogen after they had been hysterectomized. The survival periods of the corpora lutea in all the experimental animals were carefully determined by laparotomy. The results are outlined below in respect to each of the above-listed groups of animals.

Group 1. The survival period of the corpora lutea in pseudopregnant rabbits was lengthened by about 11 days more than average following hysterectomy.

Group 2. Auto-transplantation of the uterus in hysterectomized-pseudopregnant rabbits shortened the life of the corpora lutea approximately to that of normal pseudopregnancy.

Group 3. If the regression of the corpora lutea in pseudopregnant animals is due to a gradual decrease in estrogen concentration, then an increase should prevent the regression. It was found that with one mg. of estrone daily, the corpora lutea could be adequately maintained as long as the injections lasted, and a complete regression of the corpora lutea occurred 3 or 4 days after injections were stopped.

Group 4. The removal of the uterus together with the uterine contents in pregnant animals causes a shortening of the functional life of the corpora lutea, no corpora surviving as long as those of normal pregnancy. These results suggest that the mechanism of functional regulation of the corpus luteum in pregnant animals is different from that in pseudopregnancy.

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one of the clearest demonstrations of this hepatic function. In the present paper the authors describe the estrogenic effects of stilbestrol and estrone in rats whose enterohepatic circulation was interrupted by severing their bile ducts.

The estrogens used for this study were estrone and stilbestrol; the dosage was one mg. dissolved in peanut oil given at a single injection either intraperitoneally or subcutaneously. Estrus was determined daily by vaginal lavage. The rats used in the experiments had the bile ducts severed and the ovaries removed. The controls were merely oöphorectomized.

The estrogenic effect of stilbestrol was as usual more prolonged than that obtained with a similar amount of estrone. When the enterohepatic circulation of estrogens was eliminated by severing the bile duct the estrogenic effects of estrone and stilbestrol were definitely prolonged. Since the result of cutting the bile duct was to prolong estrus, it seems evident that the enterohepatic circulation of stilbestrol does not account for the known long-lasting effect of this estrogen.

After the bile duct was severed, both estrone and stilbestrol were especially prolonged in action following subcutaneous injections. The authors believe that this implies delayed absorption, rather than delayed destruction of these estrogens by the liver.

(It appears to be definitely established that the liver is instrumental in the destruction of the estrogens, and this is supported by the experiments of the authors. Aside from this, however, they seem to indicate that the more prolonged estrogenic effect of stilbestrol is not due to any lesser degree of destruction of this substance by the liver.—Ed.)

## THE STIMULATING ACTION OF ESTROGEN ON RELEASE OF LUTEINIZING HORMONE

A. A. HELLBAUM AND R. O. GREEP

Federation Proc., 5: 182-183, 1946

The pituitaries of adult female rats, under normal estrogen influence, stimulate moderate luteinization in normal and hypophysectomized recipients. On the other hand, the pituitaries of adult female rats whose estrogen influence has been removed by oöphorectomy, stimulate extensive luteinization of the recipient ovaries. This indicates that the luteinizing factor is not liberated in the absence of estrogen, but remains stored within the pituitary gland.

That estrogen releases the luteinizing factor is also suggested by the type of response produced by pituitaries from oöphorectomized adult female rats which have been injected with estradiol benzoate daily for 30 to 45 days. The pituitaries of these animals stimulate follicular development but no corpora lutea, the luteinizing factor having been removed under the influence of the estrogen treatment.

Group 5. In view of the findings in the above group of animals, it is evident that some tissue within the uterus must be responsible for maintenance of the corpora lutea in pregnancy, and it is probable that the placenta may be the organ concerned. When hysterectomized-pregnant rabbits received placental implants, the life of the corpora lutea was much lengthened, being maintained as long as in normal pregnancy.

Group 6. To obtain a clearer demonstration of the possibility that the placenta provides a stimulus for the maintenance of the corpus luteum, the placentae of pregnant rabbits were removed, leaving the uterus intact. The corpora lutea showed a close similarity to those observed in the hysterectomized-pregnant animals.

Group 7. It was found that the corpus luteum in pregnant rabbits is sensitive to the administration of estrogen as it is in pseudopregnant animals. Thus, the corpora lutea of hysterectomized-pregnant rabbits were well maintained with one mg. of estrone daily, and completely regressed one week after stopping the injections.

These experiments suggest that the substance produced by the placental tissue which apparently maintains the corpus luteum in pregnancy is of the nature of an estrogen. The authors believe that estrogen may be the common factor for the maintenance of the corpus luteum in both pregnant and pseudopregnant conditions. This hypothesis is handicapped by the fact that the presence of estrogenic hormones in the placental tissue of the rabbit has not been demonstrated.

(That some sort of interrelationship exists between the ovary and the uterus, other than the known effects of the ovarian hormones upon the latter, has long been believed by many gynecologists. Even an endometrial or uterine hormone has been postulated by some, but in spite of considerable experimental study, its existence has never been demonstrated. There are a number of clinical facts which suggest a reciprocal relationship between the two organs. For example, vasomotor phenomena are not infrequently seen after hysterectomy even if the ovaries are conserved, though usually much less severe and less prolonged than if both ovaries are removed.

The paper of Chu and You is concerned with this interrelationship during pregnancy, and confirms its existence. It is of interest to note that it is to estrogen, as is probably true in the non-pregnant animal, that they ascribe the role of maintaining the corpus luteum of pregnancy, rather than to the chorionic gonadotrophic hormone, which some have thought to be more important in this connection.—Ed.)

## ENTEROHEPATIC CIRCULATION OF OESTROGENS

F. E. EMERY AND H. E. JOYCE

J. Endocrinol., 4: 371-374, 1946

Strong evidence has been presented in the literature that the liver destroys the activity of estrogens, the inactivation of estrogens by isolated liver tissue being

## THE ORAL USE OF HEXESTROL FOR ESTROGEN DEFICIENCY

FLOYD E. HARDING

Am. J. Obst. &amp; Gynec., 51: 660-665, 1946

Ninety patients suffering from the menopausal syndrome were treated with hexestrol in order that a clinical comparison might be made with other orally administered natural and synthetic estrogens. The hexestrol used in this study consisted of uncoated 0.2 mg., 1 mg. and 3 mg. tablets. The efficacy of treatment with hexestrol was judged by the amount of clinical improvement observed, particularly by the duration, frequency and intensity of hot flushes.

Of the 90 patients treated with hexestrol, 32 patients had natural menopause, 25 had artificial menopause and 33 had other conditions and an associated ovarian deficiency.

Satisfactory results were obtained with hexestrol in all instances; the average patient in this series required 1 to 2 mg. doses per day. Some patients required a larger dose, while others were relieved with 0.5 mg. There was a low incidence of toxic reactions (3 to 6 per cent) without apparent permanent harm from the dosages used. The severity of unfavorable effects depended upon the dosage administered. The tablets were used also as a therapeutic test to help differentiate estrogen deficiency from other conditions.

Hexestrol shared with diethylstilbestrol the advantage of being inexpensive. The author suggests that this synthetic estrogenic substance would be more efficacious for the treatment of some patients than diethylstilbestrol.

A comparison with 3 other orally administered substances showed that the undesirable effects upon menstruation were less frequent with hexestrol therapy than with the other 3 substances.

(A great many comparative studies of this sort have been published, with not a great deal of difference in result. Everyone is agreed that diethylstilbestrol is effective, but that a certain proportion, probably 10 to 15 per cent, of patients cannot take it because of unpleasant toxic symptoms. Hexestrol is likewise effective, with probably a somewhat lesser proportion of unpleasant side effects, although approximately twice as large a dose is required as with stilbestrol. A considerable number of other effective oral estrogens are available, such as etbinyl estradiol, premarin, henzestrol, etc.—Ed.)

## PROGESTERONE THERAPY IN UTERINE FIBROMYOMA

AUBREY L. GOODMAN

J. Clin. Endocrinol., 6: 402-408, 1946

The present study is based on the work of Lipschütz and his co-workers who, postulating that progesterone produced in the body may react synergistically with estrogen on the uterine mucosa but also have an antagonistic action, in-

(These experiments bear out the general concept that the pituitary function is of the so-called one-two type, as is true also of the ovaries. Moreover, they seem to confirm the idea that the luteinizing factor is motivated by the increasing estrogen production. Incidentally, it is this special phase of the pituitary cycle, where there is considerable follicle-ripening factor and just a "pinch" of the luteinizing principle, which is believed to call forth ovulation in the ovary.—Ed.)

## PRACTICAL GYNÉCOLOGICAL ENDOCRINOLOGY

E. STEWART TAYLOR

Rocky Mountain M. J., 43: 292-299, 1946

The author presents a short review of the female hormones, gives an outline for the practice of office gynecology and clarifies the correct place of the various trade-name hormones in this scheme. At the end of the article there appears a chart which gives the scientific name and use of the various hormone drugs, their proprietary label and their manufacturer.

Practical application of the various hormones is outlined for the following problems: gonorrheal vaginitis, senile vaginitis, dysmenorrhea, threatened or habitual abortions, sterility, functional uterine bleeding, menstrual headaches, premenstrual tension, primary and secondary amenorrhea and hypomenorrhea, premenstrual sore breasts, chronic cystic mastitis, frigidity, menopause and inhibition of lactation.

From the present discussion it may be deduced that estrogenic substances are the most dependable and most widely used of the hormonal preparations. Estradiol is the compound found in ovarian follicular fluid. Estrone and estriol are excretory products of estradiol, found in the pregnancy urine. Estradiol benzoate and estradiol dipropionate have similar action to estradiol, estrone and estriol, except that they are much more potent and more prolonged in action. When quick, short-lived results are desired, one should choose estrone. Oral preparations of the natural estrogens need to be given in 5 times the dosage that is required of the hypodermic preparations. The estradiol benzoate and estradiol di-propionate are synthetic estrogens.

Authorities warn of possible carcinogenic effects of estrogens and estrogen-active substances such as stilbestrol. The author states that surely those patients who have had, or have cancer, should never be given estrogens or stilbestrol. If hormones are used when indicated and in the dosages outlined in this paper, the carcinogenic activity need not be feared. Prolonged administration of estrogen or stilbestrol in large quantities is to be condemned.

(A satisfactory brief review of a broad field.—Ed.)

follow-up, but probably also proved to be pregnant. In 42 instances menstruation followed the Prostigmin injections and in none of them did evidence of pregnancy develop subsequently. While these data are not extensive, they suggest that Prostigmin as a diagnostic agent for pregnancy may be depended upon for an accuracy of almost 100 per cent. The procedure was found simple and inexpensive. The concurrent use of other common "biological" tests is indicated in only a very small number of borderline cases.

(There have been a large number of reports on the prostigmin pregnancy test in recent years, some pro and some con. The proportion of the latter, however, is sufficiently great to have placed it for the present in a plane of accuracy definitely below that of the Friedman, Aschheim-Zondek and Hogben tests. It is certainly simple and inexpensive, and if the universal experience were that it is almost 100 per cent accurate, as the author found in his series of 56 cases, it would no doubt have achieved far wider employment than it has. Further observations over the next few years will probably crystallize its status more sharply than is possible as yet.—Ed.)

## OBESITY-PITUITARY DEFICIENCY IN THE FEMALE

RALPH G. BONTME

M. Clin. North America, 30: 683-706, 1946

In this paper the author presents his clinical observations during a 5-year period while treating a group of individuals who complained chiefly of obesity and symptoms related to thyropituitary deficiency, and the conclusions drawn from that treatment.

Obesity-thyropituitary deficiency is characterized by a uniform triad of signs and symptoms which include obesity, menstrual disturbances (hypogonadism) and symptoms of pituitary deficiency. The obesity may be slight, the genital involvement may be difficult to evaluate and the associated symptoms may be masked by degree, by temperament, by the compensatory mechanisms of the body, and by a total lack of uniformity. The present report concerns 52 female patients who were selected for presentation because they illustrate gonadotropic response (menstrual phenomena). Except for this demonstrability, similar results were obtained in males and females of all types and ages.

The patients in the present series all were within the age limits when full ovarian function is to be expected. Most of the patients exhibited the typical pituitary fat distribution described by Goldzieher, Hamblen, and Beck, and others. The patients were divided into 4 groups according to menstrual disorders, and where there were dual characteristics, the more common decided in which group the patient was classified. Eleven patients suffered from dysmenorrhea, 13 patients from amenorrhea, 20 patients from hypomenorrhea and oligomenorrhea, and 8 patients from hypermenorrhea and polymenorrhea. The menstrual disturbances were accompanied by numerous miscellaneous symptoms including headache, fatigability, somnolence, emotional instability, mental sluggishness, dyspnea, precordial pain, backache, nocturia, polydipsia, poly-

vestigated the preventive action of several steroids, including progesterone, upon experimentally produced fibroids in the guinea pig. They observed that the fibroids decreased and disappeared with this therapy.

Seven patients having fibromata uteri, clinically diagnosed, were treated by injections of progesterone. A decrease in size of the tumor or of the uterus was observed in all cases.

All of these patients were charity cases, and none has returned for follow-up study since the relief of symptoms; thus, it is emphasized that the author does not claim a final therapeutic effect of progesterone in fibromyomata. Neither is progesterone offered as a substitute for the presently accepted methods of surgical or radiation therapy of fibromyoma. This paper aims simply to encourage further investigation of the possible therapeutic value of progesterone treatment in such conditions.

(I do not believe that there is any sound basis for this plan of therapy, or that the experimental studies of Lipschütz and his co-workers offer any justification for its employment in the human. The tumors produced in guinea pigs by estrogen administration are not myomas but fibromas, nor do they occur in the uterus but rather in the connective tissues of both the pelvis and the general abdomen. They are not true tumors, since they disappear after the estrogen is withdrawn, or after administration of progesterone. But this, as far as I can see, has nothing to do with the etiology of uterine myoma, as Lipschütz himself was only too ready to concede when I discussed the matter with him on the occasion of his visit to this country some years ago. Moreover, with a large proportion of uterine myomas, probably the majority, ovulation occurs quite normally, as is not infrequently attested by the occurrence of pregnancy. The tumors, in other words, may continue to grow even though the patient's corpora lutea are supplying her with progesterone. The author will have to produce much more evidence than his impressions of a possible effect in 7 cases, especially since his premise seems so unsound.—Ed.)

## CLINICAL USE OF PROSTIGMIN AS AN IDEAL OFFICE PROCEDURE IN DETERMINING PREGNANCY

ADOLPH L. NATENSHON

West. J. Surg., 54: 149-152, 1946

The present study comprises 56 patients in whom prostigmin was employed as a test for determining pregnancy. None of these patients had any definite pelvic pathology, nor was the test used in women with signs or symptoms suggesting the menopause. The Friedman test, or some similar procedure, was used supplementally in questionable ectopic pregnancies, postpartum delay, beginning menopause and in other cases with irregular menstrual histories or suspected pelvic abnormality. Each patient received 1 cc. of Prostigmin Methylsulfate 1:2000 intramuscularly on each of 3 successive days. The test was carried out in 61 instances. In 19 instances a positive result was obtained, i.e., menstruation did not ensue, and all but 3 of the patients are known to have undergone delivery or abortion. The 3 patients in question never returned for

that the incidence of uterine atrophy in 3000 labors and puerpera was not more than one per cent. According to the literature, the patient's chief complaint is not the amenorrhea, despite the fact that breast feeding has been discontinued for several months, but she complains of abdominal pain, sensations of active movement in the abdomen, backache and hysterical manifestations. Usually there are no inflammatory changes, but atrophy of the uterus and cervix are present. In the majority of cases the ovaries are small and atrophic. Frommel recommended prophylaxis against numerous successive pregnancies, detection of the abnormal involution early in the puerperium, followed by immediate weaning of the infant. In regard to therapy, he suggested improved nutrition, hot sitz baths, insertion of pessaries to irritate the uterus and correction of anemias.

The author presents the case of a 28 year old woman who was first seen on March 20, 1944, complaining of amenorrhea with continued lactation since the birth of her only child on December 28, 1942. She also complained of generalized malaise and vague lower abdominal pains.

Physical examination revealed a small, undernourished Negro woman from whose nipples milk could easily be expressed. The cervix was in normal position, firm in consistency and markedly reduced in size. The uterus was also markedly reduced in size and its walls appeared abnormally thin. The uterine cavity measured 4.5 cm. in depth. Both ovaries were palpable and relatively small. An endometrial biopsy revealed atrophic endometrium. The patient was placed on stilbestrol, 5 mg. twice daily for 5 days.

On June 29, the patient reported the return of menstruation with scant flow on June 12 and 13. Examination revealed a uterus and cervix normal in size and consistency. Lactation was still present to a marked degree. Stilbestrol was administered as previously and 5 grains of ferrous sulfate 3 times a day was prescribed.

From July through December, 1944, the patient menstruated twice monthly for a period of 3 days. In January and February, 1945, the menses occurred once monthly for 4 days. The breasts still contained some watery secretion. The cervix and uterus were normal, the uterine cavity measuring 8.5 cm. in depth. Both adnexal areas were negative. When seen in March, 1946, the patient stated that her periods had been regular every 28 days for the past year.

(Although the Chiari-Frommel syndrome is a rare one, it is of interest that in less than 2 years there have been two American reports of such cases, that of Mendel, herein abstracted, and that of Potter (*Am. J. Obst. & Gynec.*, 42:276, 1944). While the exact mechanism of this disorder is not clear, it would seem, especially from the common association of amenorrhea and persistent lactation, that the dysfunction is in the pituitary. The tendency appears to be toward spontaneous readjustment of the endocrine mechanism after a variable length of time.—Ed.)

phagia, loss of libido, hirsutism, acne and insomnia. Basal metabolic rates varied from minus 23 per cent to plus 50 per cent. Sugar tolerance, cholesterol and uric acid estimations tended to be high, while relative lymphocytosis was frequently noted.

Treatment consisted of diet, desiccated thyroid by mouth and anterior lobe pituitary extract by injection. No other therapeutic measures were taken. A diet high in protein, low in carbohydrate and low in fat content was prescribed for all patients. One grain of desiccated thyroid daily by mouth was prescribed. In the presence of an unchanged pulse rate or a pulse rate below 90, the dosage was increased until the point of tolerance had been reached. A water-soluble unfractionated extract of the anterior lobe of the pituitary was used.

This regime of treatment yielded uniform and predictable responses. As a rule, improvement was noted within one or 2 weeks. General symptoms vanished within a month. Many patients lost a good deal of weight, some lost none, but no patient gained weight. The alterations that took place in the menstrual phenomena in a relatively short time were almost dramatic. It was found that, after normalization, short periods of treatment at determined intervals helped to maintain normalcy. 3 figures.

(The author speaks of these patients as showing thyropituitary deficiency, although he says that the basal rates in some were as high as plus 50 per cent. Incidentally, many errors are made in basal metabolic tests, especially in obese women. Cases of one of the general types which he describes, showing obesity of a characteristic distribution and menstrual abnormality, usually in the form of quantitative decrease or absence, are common enough, constituting the well-known adiposogenital dystrophy or Fröhlich syndrome. These are commonly explained as of pituitary origin, and there is no doubt that the amenorrhea is due to deficiency of the pituitary gonadotrophic function. But the evidence indicates that the obesity is not of pituitary origin, but is due to disturbance in the fat-metabolism centres in the parapituitary, probably hypothalamic, areas of the brain.

It is not uncommon to see this fat-metabolism disturbance only, the patient's obesity being of characteristic Fröhlich type, with no menstrual disturbance whatever, and often with normal fertility. The basal rate in these patients is usually normal or slightly subnormal. Diet and thyroid are the mainstays in treatment. I doubt whether anterior lobe extract is of any value in "redistribution" of the fat, as Beck and others have claimed. It is usually combined with thyroid, and it is the latter which is probably more effective in the reduction of weight. It seems unwise to try to subdivide these patients on the basis of menstrual disturbances, which in some cases are concomitant rather than characteristic. This would certainly seem to be true of dysmenorrhea.—Ed.)

## CHIARI-FROMMEL SYNDROME; AN HISTORICAL REVIEW WITH CASE REPORT

EVRI B. MENDEL

Am. J. Obst. & Gynec., 51: 889-892, 1946

Cases of the rare syndrome of atrophy of the uterus and ovaries associated with persistent lactation have been reported infrequently. Frommel, in 1882, found

breeding season in normal acting macaques. In a series of convincing protocols the authors present evidence based on changes in the color of the sex skin that ovulation in the macaque is not infrequently delayed many days.

There are reasons for believing that delayed ovulation also occurs in women. The most convincing are to be found in Hartman's review of normal, early pregnancies with exceptionally reliable clinical histories (*Time of Ovulation in Women*, Baltimore, 1936, Williams & Wilkins). In 18 of the 54, that is in one-third, ovulation occurred between the 18th and 24th days of the cycle. Other reports show similar findings.

These observations obviously have an important bearing on the dependability of the "safe period" in contraceptive procedure. A woman who requests advice on this subject may ask, "What are the chances in my case that an ovulation will occur 3 or more weeks after a period?" There is no pat answer even though she has kept a menstrual calendar for many years. Many "failures of the safe period" can be ascribed to our ignorance of the incidence of delayed ovulation in women.

(While the truth of Fraenkel's old dictum that the only thing regular about menstruation is its irregularity, has long been recognized, I venture to say that most gynecologists still feel that in most women the variations in the cycle length would be between 25 and 31 days, and yet 25 per cent fall outside this modal group, according to the British study which the authors quote.

There has been much discussion as to whether it is the pre- or post-menstrual phase which is subject to variations in length, with apparently wide acceptance in recent years of the belief that the follicle phase is the variable one while the corpus luteum phase is of fairly fixed duration. The Ogino method of birth-control is based on this idea. But the present study yields disillusioning results, showing that either phase may exhibit considerable variation.—Ed.)

## A TEST FOR DETERMINING THE TIME OF OVULATION AND CONCEPTION IN WOMEN

EDMOND J. FARRIS

*Am. Obst. & Gynec.*, 52: 14-27, 1946

The author describes a test for detecting the time of ovulation based on the presence of hyperemia in the ovary of the immature rat after injection with the patient's urine. Evidence is adduced to show that this reaction is due to very small amounts of gonadotrophin in the urine of women at the time of ovulation.

The details of the test are as follows: Urine passed on arising on the morning is employed. The test animal is an immature Wistar rat between 22 and 25 days of age, and weighing between 30 and 50 grams. Two cc. of the urine are injected subcutaneously into each of two animals. At the end of two hours the animals are killed by means of illuminating gas. Their abdomens are opened immediately. Each ovary is inspected and its degree of redness compared with the colors of a Munsell color chart under standardized lighting conditions. The

## THE MENSTRUAL CYCLE

### DELAYED OVULATION, A SIGNIFICANT FACTOR IN THE VARIABILITY OF THE MENSTRUAL CYCLE

I. ROSSMAN AND G. W. BARTELMER

*Am. Jour. Obstet. & Gynec.*, 52: 29-33, 1946

Sufficient accurate data on the menstrual cycle have been accumulated to demonstrate that a regularly recurrent 28-day cycle is most unusual. The extent to which fluctuations in cycle length occur has had a thorough analysis by Gunn, Jenkin and Gunn (*J. Obst. & Gynaec. Brit. Emp.*, 44: 839, 1937) who found, in a group of 979 women studied, that only 9 per cent belonged to the extremely regular type with differences of 5 days or less between the longest and shortest cycle. More than 20 per cent fell outside the modal group in which cycles averaged 25 to 31 days. It appears that any woman may have an unusually long or short cycle at any time, and the chances that two successive cycles will be of equal length are negligible.

It is the purpose of this paper to inquire into the causes of these menstrual irregularities as exemplified by the macaque. Before reporting their own original observations, which have to do with the preovulatory phase of the cycle, the authors recall that the postovulatory phase is subject to considerable variation, Hartman having found that this phase in the macaque ranged from 6 to 23 days, most cases falling between 9 and 17 days. (*Am. Jour. Obstet. & Gynec.*, 26: 600, 1933.)

The irregularity of the postovulatory phase can be readily explained by the findings of Markee (*Contrib. to Embryol.* 95, Vol. 18, Carnegie Inst. Wash. Pub. 363: 79, 1926). One of the outstanding findings of his studies of endometrium transplanted to the anterior chamber of the eye in macaques is the appearance of a profound premenstrual ischemia. This varied both in duration and intensity, appearing as much as 5 days before the onset of menstruation or only one day before. If we correlate this ischemia with the decline in activity of the corpus luteum, it would seem that this organ in the absence of pregnancy may "fail" suddenly or completely. This would obviously account for a several days difference in the duration of the postovulatory phase. It is probable that similar differences occur in the human species where similar differences are found in menstruating mucous membranes.

The present report is concerned with the fact that delayed ovulation is not rare in the macaque and may account for prolongations in the preovulatory phase of the cycle. Markee states that after the end of a menstrual period the flow of blood and the growth of endometrial transplants may be promptly accelerated, or there may be a postmenstrual "resting" period lasting up to 10 days. The present authors have observed postmenstrual phases lasting much longer. These showed little evidence of endocrine activity but occurred during the

breeding season in normal acting macaques. In a series of convincing protocols the authors present evidence based on changes in the color of the sex skin that ovulation in the macaque is not infrequently delayed many days.

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reaction is said to be positive if one ovary alone or both ovaries show a definite hyperemia. The color of the test is determined in two different months for each individual. The day for starting the test depends on the length and regularity of the patient's cycles. *The testing period covers the 5 or 6 days preceding the anticipated date of ovulation, the ovulation period and three days following it.* During the testing period of both months coitus is interdicted because it produces urinary changes which cause a hyperemia in the rat ovary.

Observations were made upon 100 women. Of these, 12 were unmarried and 88 were married. Of the latter, 76 wished to become pregnant. Fifty of the latter had been inseminated artificially for periods varying from a few months to several years with no conceptions resulting. The reactions were classified as either normal or abnormal. In the case of a normal reaction there is a definite deepening of the color of the rat ovary for 3 or 4 consecutive days near the middle of the cycle. In abnormal reactions there is either no color developed at all or color for only a day or two.

The majority of the patients showed a normal color reaction month after month. The reactions occurred earlier in the shorter cycles than in the longer ones. Thus, in a patient with a 21 day cycle the hyperemia occurred on the 6th, 7th and 8th days, while in a woman with a 33 day cycle, hyperemia was not present until days 15, 16, 17 and 18. A number of women with normal reactions became pregnant. None experiencing abnormal reactions did so. Ten became pregnant when coitus took place on the 3rd or 4th day of consecutive color reaction. Of 50 patients who were being artificially inseminated at frequent intervals without success, only 11 showed normal reactions. Eight of these 11 women conceived after the insemination date was chosen according to the test.

One of the chief values of the test lies in the fact that it indicates the beginning of the period of ovulation, which makes it possible to time intercourse for the single day during that period when it is most likely to be fruitful. Pregnancies have resulted in different cases when coitus took place on days 2, 3 and 4 of the color reaction. In most instances, day 3 has been advised.

(Even if the results of these studies should be confirmed by other investigators, it is difficult to believe that the method would ever achieve any wide clinical employment.—Ed.)

## ETIOPATHOGENESIS AND TREATMENT OF MENOMETRORRHAGIAS

NARCISO AMIGO DE BONET

Toko-Ginecologia Practica (Madrid, Spain), 5: 192-206, 1946

In a brief review, the author describes the various causes of menometrorrhagias. One of these, the so-called metropathia hemorrhagica, is characterized

by cystic glandular hyperplasia of the endometrium due to follicular persistence in the ovaries, and in 90 per cent of the cases appears in women beyond the age of 37 and in 5 per cent below 20. Pathologically the ovaries show no recent corpus luteum but follicular cysts are frequently present. Follicular hyperactivity seems to play an important role in its pathogenesis.

The duration of the follicular phase of the menstrual cycle depends on the number of follicles growing simultaneously and on the rapidity with which they undergo atresia. As a matter of fact, it is quite possible that the corpus luteum duration depends on the greater or smaller number of atretic follicles and on the speed of their retrogression.

Metropathia hemorrhagica may be caused by the persistence of a follicle that does not rupture and, therefore, does not transform into a corpus luteum (Schroeder), or by several succeeding phases of growth and retrogression of follicles (Meyer). In either event the result is the same: persistence of the follicular phase in the ovary, without formation of corpus luteum, and persistence of the proliferative phase in the endometrium, with symptoms of hyperactivity.

What causes the lack of follicular rupture still remains a matter of discussion. It seems that various factors may be concerned. In this condition the pituitary seems to produce large amounts of gonadotrophin. The ovule itself undoubtedly plays an important role in the pathogenesis of glandular cystic hyperplasia. As a matter of fact, this condition usually appears in two distinct periods of life, i. e., when the ovules start to mature and when sexual activity starts to decline.

Other causes of metrorrhagias are submucous fibroids, uterine polyp (mucoid or fibroid type), placental polyp, ectopic pregnancy which gives rise to bleeding in 85 per cent of the cases at the time that tubal rupture or abortion occurs, and in some instances even before. The latter is a dyshormonal type of bleeding.

Incomplete abortion, hydatidiform mole and chorioepithelioma are listed as other causes of metrorrhagias. Premenstrual bleeding is due to alterations occurring in the functional layer of the endometrium, so that some vessels rupture and give rise to small hemorrhages. Postmenstrual bleeding, on the other hand, is related to alterations occurring in the estrogenic phase of the cycle.

Climacteric bleeding is produced by rapid maturation of ovules and follicles, which leads to the production of incomplete cycles, due to insufficient maturation of the ovule and formation of corpus luteum. This type of bleeding can easily be mistaken for that arising in carcinoma of the cervix. Beyond the age of 40 years, 50 per cent of metrorrhagias are caused by uterine cancer, and beyond the fiftieth this percentage goes up to 95.

Treatment of menometrorrhagias varies according to its etiology. In those of psychic origin, psychotherapy is advised together with vitamin B1 (2.500 I. U. intravenous, daily, until a total amount of 12.500 I. U. is reached). When caused by pituitary disturbances, usually these are the result of lack of the posterior hormone or oxytocic principle; therefore, pituitrin is given 10.000 I. U. daily.

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Treatment is based on the etiological factor. In the congenital group there are cases showing some developmental abnormality, such as the presence of a rudimentary uterine cornu, stenosis of the external os of the cervix, etc.. Many of such cases are cured by marriage or childbirth.

When dysmenorrhea is related to endocrine disturbances, sexual hormones are indicated. The author uses estrogen in doses higher than the Americans usually do: 50,000 to 150,000 units throughout the first phase of the menstrual cycle, starting soon after the last day of menstruation. If this proves to be unsatisfactory, estrogen is also given throughout the second half of the cycle. If this plan of treatment fails, testosterone is given during the first half of the cycle. Thyroid is used if there are signs of thyroid deficiency.

In some cases x-ray of the pituitary in stimulant doses, in order to promote greater secretion of gonadotrophins and, thereby, of sexual hormones, furnishes good results. For intractable cases, surgical procedures are advocated: dilatation of the cervix or presacral sympathectomy.

(The author's discussion of the treatment of dysmenorrhea is concerned chiefly with endocrine measures, which many of us are finding less and less effective with experience, and employing less and less in our practices. In severe cases there can be no criticism of the employment of either estrogens or androgens as a part of the treatment, but failure is likely to result unless these are combined with constitutional and psychotherapeutic measures. These alone are likely to suffice in the milder cases, with perhaps the addition of simple analgesics. There would seem to be no intelligent reason to justify x-ray treatment of the hypophysis, and if any benefit has been noted from this method, I should think it would be explained on a psychic basis. Presacral sympathectomy has a place in the treatment of severe and intractable cases, but it should not be resorted to if simpler and safer measures make the patient reasonably comfortable, as they usually will.—Ed.)

## SYNDROME CHARACTERISTIC FOR MENOPAUSE, OVARIAN HYPOFUNCTION AND CASTRATION IN THE THE HUMAN FEMALE

AUGUST A. WERNER

J. Missouri M. A., 37: 311-315, 1946

The present paper is based upon an analysis of the objective signs and subjective symptoms presented by 197 women having deficiency or absence of the ovarian follicular hormone. The group consists of 53 castrates, 96 women in the menopause and 48 having involutional melancholia. The subjective symptoms are classified as nervous, circulatory and general. Nervous symptoms include tension, excitability, headaches, mental depression, decreased memory and concentration, formication, insomnia and somnolence. Circulatory symptoms include hot flushes, tachycardia, vertigo, tinnitus, scotomata, cold extremities and low pulse and blood pressure. General symptoms include lassitude, fatigability, constipation and vague pains.

This group of symptoms is primarily initiated by ovarian hypofunction, the

mon hemostatic substances together with calcium and vitamin C. If no effect is obtained in spite of this medication, progesterone is given during the second half of the cycle (2 U. C. daily) or else prolan (1500-2000 U. R.), which acts as a luteinizing factor in such doses.

If these young patients show a hypoplastic uterus, estrogen is indicated, sometimes associated with pituitrin, or at other times with thyroïdin. In emergency cases, intravenous administration of a 1 to 5 per cent "red Congo" solution may prove to be useful. If bleeding still persists, blood transfusions and sometimes irradiation of the spleen and liver are indicated.

In case the bleeding should recur some months later, radium ought to be used in order to obtain a period of amenorrhea of 4 or 5 months duration, which is usually followed by normal periods.

For cases of glandular cystic hyperplasia, mainly in young patients, hemostatic substances should first be used. If they should fail, then hormonotherapy has its indication. Progesterone is given in large doses (100 mgms. a week). If bleeding is just beginning, estrogen can be used in order to help epithelization of the endometrium. Transfusions of pregnant woman's blood can also be helpful, as it contains gonadotrophin.

When medical treatment fails, a curettage is indicated, which yields 50 per cent of cures, besides being an excellent diagnostic procedure. X-ray can be used in women approaching the menopause in order to abolish ovarian function. The same can be said for intra-uterine radium. Climacteric bleeding is treated like metropathia hemorrhagica.

For bleeding caused by carcinoma of the uterus, chronic pelvic inflammatory disease, fibroids, and ovarian tumors, especially the granulosa cell carcinoma, treatment varies in each case according to the cause.

(A rather comprehensive discussion of an important subject. While all will agree that the majority of functional bleeding cases occur in the menopausal and pre-menopausal years, I do not believe that as many as 90 per cent occur after 37, or as few as 5 per cent below 20. It is of interest to note that the author still uses posterior pituitary preparations in some cases. These were available long before we had ovarian or androgenic preparations of any efficacy, and I myself used them frequently in those days, with apparent benefit in not a few. In certain emergency cases he uses red Congo solution, and I wonder what the rationale of this may be, as I had never heard of this method of treatment. No further comment on this paper will be made, since the Editor's ideas on the subject are set forth in the review on Functional Bleeding, in this issue of the Survey.—Ed.)

## ETIOPATHOGENESIS AND TREATMENT OF DYSMENORRHEA

AMIGO DE BONET

Toko-Ginecologia Practica 5: 1-6, 1946

The author describes the well known different types of dysmenorrhea, which are usually classified in two main groups: congenital and acquired.

3. Artificial menopause is frequently followed by complaints of an arthralgic nature.
4. Favorable response of such patients to estrogenic therapy.
5. Favorable effect of pregnancy upon rheumatoid arthritis.
6. The arthritic process is usually limited to the period of transition during the menopause, usually subsiding after a few years without exhibiting residual changes.
7. Exacerbation of arthritic episodes during the menstrual period at the time of the menstrual cycle when estrogens are at a low level.

Other important factors which deserve consideration are thyroid hypofunction and general increase in weight. These conditions are frequently present during the menopause and should not be neglected in the treatment of menopausal arthritis.

The therapeutic approach to menopausal arthritis or arthralgia revolves around the attempt to correct the constitutional disturbances present during the menopause. Therapy with estrogenic substances must be relatively high, and dosage levels should not be judged entirely by maturation of the vaginal smear cells, but by the subjective improvement and lessening of complaints. A therapeutic trial, employing doses such as 2000 to 10,000 R.U. of estradiol benzoate or its equivalent every 7 to 10 days for a period of several months, is advisable.

Adjunctive thyroid therapy should be used in specific instances. To avoid an untoward response of the patient to this therapy, it is advisable to place the patient on small doses of  $\frac{1}{4}$  to  $\frac{1}{2}$  grain of thyroid daily and, in the event that no evidence of intolerance is observed, the dose may be gradually increased until the desired clinical response is approached. The rationale for thyroid therapy is based on the following observations:

1. Thyroid therapy tends to correct certain physiological upsets at the time of the menopause and promotes an attempt to equalize the processes of catabolism and anabolism.
2. Estrogenic therapy may have an inhibitory effect upon the metabolic principle of the thyroid gland either by inhibiting the thyrotrophic hormone of the hypophysis or by inhibiting the metabolic hormone itself. Replacement therapy with thyroid will counteract the physiological depression of the thyroid gland.

Patients with arthralgia associated with the symptoms of the menopause may show no demonstrable pathologic changes in the joints. In those who do show changes, atrophic arthritis is more common than the hypertrophic variety.

(The question of menopausal arthritis has been discussed by both gynecologists and internists for many years, and the consensus among both seems to be that such an entity does exist, though not extremely common. Most frequently it involves the knee joints, and at times there is definite swelling, especially above the inner condyles. Estrogenic therapy seems to be a helpful addition to the usual therapy of arthritis. I have had no experience with thyroid therapy in cases of this sort, and it may be of value, though the rationale for its use, as suggested by the authors, is rather speculative.—Ed.)

ovarian hypofunction resulting from the causes enumerated. There may be secondary disturbances of function of the pituitary, the thyroid and the adrenals, with consequent imbalance of the equilibrium normally existing between the 2 divisions of the autonomic nervous system. The symptoms occur in castrates and women at the menopause. Many younger women who have irregular and scanty menstruation or amenorrhea during the menacme also develop this typical syndrome. In such circumstances and when there is not much menstrual disorder, one may fail to recognize ovarian hypofunction as a possible cause.

This same train of symptoms is found with striking parallelism, but more severe, in involutional melancholia. Involutional melancholia is an exaggeration of the menopausal syndrome and has the same etiology.

It is concluded that all of these groups of patients derive the greatest benefit from the administration of estrogenic hormones.

(Although not emphasized in this paper, it is quite certain that in this group of 197 women there must have been many who suffered very few or perhaps none of the horrendous list of symptoms enumerated above. Not all of these are hormone deprivation symptoms, nor most of them, and it is hoped that the author does not mean that this formidable array constitutes the characteristic picture of the menopause. It is rather startling to see that he diagnosed involutional melancholia in fully one fourth of his patients, and it is obvious that his criteria for such a diagnosis are much looser than those of most gynecologists. I am sure that I have not made such a diagnosis 48 times in many times 197 menopausal women whom I have seen.

The proper conception of this term, according to the psychiatrists with whom I have discussed the problem, is that it should be applied to a genuine psychopathy in the involutional period of life, occurring in either sex, and not causally related to the menopause. Any associated vasomotor symptoms may be helped by estrogenic therapy, but the actual psychopathy calls for psychiatric treatment. It does not seem to me that there is any justification in applying this designation to "exaggeration of the menopausal symptoms" or that it has the same etiology.—Ed.)

## MENOPAUSAL ARTHRITIS

R. B. GREENBLATT AND H. S. KUPPERMAN

M. Clin. North America, 30: 576-583, 1946

The authors suggest that some hormonal dysfunction may be responsible for the inception or the exacerbation of many of the arthritides occurring at or after the menopause. Presumptive evidence of the relationship of the alterations in ovarian secretions to the inception of arthritic changes is based on the following observations:

1. Arthritis or arthralgia has been noted in 27 per cent of 1000 menopausal cases.

2. Data on the sex incidence of adults between the ages of 37 and 54 exhibiting arthritic complaints show that 5 times as many females as males are affected.

3. Artificial menopause is frequently followed by complaints of an arthralgic nature.

4. Favorable response of such patients to estrogenic therapy.

5. Favorable effect of pregnancy upon rheumatoid arthritis.

6. The arthritic process is usually limited to the period of transition during the menopause, usually subsiding after a few years without exhibiting residual changes.

7. Exacerbation of arthritic episodes during the menstrual period at the time of the menstrual cycle when estrogens are at a low level.

Other important factors which deserve consideration are thyroid hypofunction and general increase in weight. These conditions are frequently present during the menopause and should not be neglected in the treatment of menopausal arthritis.

The therapeutic approach to menopausal arthritis or arthralgia revolves around the attempt to correct the constitutional disturbances present during the menopause. Therapy with estrogenic substances must be relatively high, and dosage levels should not be judged entirely by maturation of the vaginal smear cells, but by the subjective improvement and lessening of complaints. A therapeutic trial, employing doses such as 2000 to 10,000 R.U. of estradiol benzoate or its equivalent every 7 to 10 days for a period of several months, is advisable.

Adjunctive thyroid therapy should be used in specific instances. To avoid an untoward response of the patient to this therapy, it is advisable to place the patient on small doses of  $\frac{1}{4}$  to  $\frac{1}{2}$  grain of thyroid daily and, in the event that no evidence of intolerance is observed, the dose may be gradually increased until the desired clinical response is approached. The rationale for thyroid therapy is based on the following observations:

1. Thyroid therapy tends to correct certain physiological upsets at the time of the menopause and promotes an attempt to equalize the processes of catabolism and anabolism.

2. Estrogenic therapy may have an inhibitory effect upon the metabolic principle of the thyroid gland either by inhibiting the thyrotrophic hormone of the hypophysis or by inhibiting the metabolic hormone itself. Replacement therapy with thyroid will counteract the physiological depression of the thyroid gland.

Patients with arthralgia associated with the symptoms of the menopause may show no demonstrable pathologic changes in the joints. In those who do show changes, atrophic arthritis is more common than the hypertrophic variety.

(The question of menopausal arthritis has been discussed by both gynecologists and internists for many years, and the consensus among both seems to be that such an entity does exist, though not extremely common. Most frequently it involves the knee joints, and at times there is definite swelling, especially above the inner condyles. Estrogenic therapy seems to be a helpful addition to the usual therapy of arthritis. I have had no experience with thyroid therapy in cases of this sort, and it may be of value, though the rationale for its use, as suggested by the authors, is rather speculative.—Ed.)

## VULVA AND VAGINA

### TUBERCULOUS ULCER OF THE VULVA

M. D. SPEISER AND H. B. GUYER

Am. J. Obst. & Gynec., 51: 718-721, 1946

The case is presented of a 35 year old Negro housewife who was admitted to the hospital with the following complaints: ulcer of right labium minus, weakness and 20-pound weight loss in past year, fever, low back pain and left sternoclavicular pain. About 5 years previously she had had a total hysterectomy and bilateral salpingo-oophorectomy. The discharge diagnosis was bilateral pyosalpingitis. Chest x-ray at that time showed increased density in the hilar regions, but both lung fields were otherwise normal. There was no familial history of tuberculosis or of contact tuberculosis.

The present illness had begun 4 months prior to admission when the patient first noticed a growth which became larger, painful and tender. During the past 3 months she had suffered from pain in the lower back and left sternoclavicular region, radiating to the left arm and chest. She also complained of nocturia, urgency and burning on urination and bladder fullness after voiding.

Physical examination revealed a poorly nourished, chronically ill woman, with evidence of weight loss. A semifluctuant, ill-defined mass was present over the sternoclavicular junction and auscultation revealed occasional wheezes in both posterior lung bases. The abdomen was moderately distended and tympanitic. Some shotty posterior cervical and axillary lymph nodes were present and the inguinal nodes were bilaterally enlarged. Pelvic examination showed a one cm. ulcer on the right labium minus; the ulcer was irregular in outline, tender, superficial, moderately clean, with a slightly raised border.

Repeated tests on sputum, gastric contents and urine were negative for tubercle bacilli, dark-field examination of the ulcer was negative and the Frei and Ducrey skin tests were negative. Chest x-ray showed enlargement of the hilar shadows and a diffuse scattering of small nodular lesions throughout both lungs. An attempt to aspirate the fluctuant area over the left sternoclavicular joint was unsuccessful due to the patient's lack of cooperation.

A provisional diagnosis of tuberculous ulcer of the vulva or early vulval carcinoma associated with a tuberculous peritonitis was made. A block excision of the right labial ulcer was done under local anesthesia and the pathological report was tuberculous ulcer of the vulva. The patient was transferred to the Tuberculous Service, but left there against advice and has not been located since. 2 figures.

(It is not clear from the data given in this report whether the vulvar infection was thought to be hematogenous or of descending type from tuberculous salpingitis. Tu-

berculosis of the vulva is exceedingly rare. While it might conceivably occur in very late stages of genital tuberculosis originating in the tube, it is more frequently explained by external infection, usually from a tuberculous husband.—Ed.)

## A CONGENITAL ANOMALY OF THE VAGINA WITH PYOCOLPOS

DANIEL J. MCSWEENEY

*Am. J. Obst. & Gynec.*, 51: 726-728, 1946

The author presents a case of congenital atresia of the vagina which is of interest because the patient experienced no menstrual difficulty suggestive of her anomaly, and also because it contributes further evidence to substantiate the dual origin of the vagina, the upper two-thirds from the müllerian system and the lower third from the urogenital sinus.

The patient was a 40 year old unmarried secretary whose menstrual history showed no dysmenorrhea or metrorrhagia. The menses had ceased about a year prior to the present hospital admission. For the past 10 years the patient had a vaginal discharge, varying from watery to purulent in character. For the past 3 weeks it was extremely foul and there had been rather steady lower abdominal pain.

Physical examination was negative except for local findings. On digital examination the vagina was felt as a rudimentary closed pouch about one inch in width and depth. Attempts to locate a sinus were unsuccessful. Rectal examination revealed the uterus high and apparently normal, and below it was felt a soft, apparently cystic mass extending to the rudimentary vagina.

At operation the uterus and adnexa were found to be normal. Extending downward from the uterus was a sac corresponding to the vagina, definitely cystic and very thin-walled in its lower aspect. A complete hysterectomy with excision of the upper vaginal sac was performed. The pathologic findings were: subacute endometritis, extreme chronic and acute cervicitis, acute and chronic vaginitis, pyometra and pyocolpos.

The construction of the 2 vaginal sacs in this case is obvious proof of the dual origin of the vagina. The arrest of the vagina at such a late stage in its embryologic development without associated abnormalities in the rest of the reproductive organs is interesting. 1 figure.

(The strange feature of this case is that the patient had menstruated normally until the age of 40, so that, even if there were a congenital stenosis in the lower portion of the vagina its later complete closure, with the development of pyocolpos, must have been due to some added factor, most likely infection followed by cicatrization. Since the patient had evidently not been previously studied, it is perhaps not even certain that a congenital stenosis had been present. In the presence of a condition which had been diagnosed as pyocolpos, one cannot but wonder why the pus accumulation was not simply drained from below,

without subjecting the patient to what would obviously be a hazardous abdominal hysterectomy under the existing conditions. As a matter of fact, the author reports that some of the foul pus escaped into the abdomen, although luckily the patient came through her ordeal safely.—Ed.)

## A METHOD OF TREATMENT FOR VAGINITIS AND CERVICITIS

SAMUEL L. SIEGLER

Am. Jour. Obst. & Gynec., 52: 1-13, 1946

A new antivaginitis jelly is described, the composition of which is as follows: sulfathiazole, 10.0%; lactic acid, 3.0%; acetic acid 1.0%; sodium tetradecyl sulfate 0.1%; polyethylene glycol 85.9%.

The acid jelly base, polyethylene glycol, has all the desired characteristics for vaginal medication. It is nonirritant and nontoxic, has excellent wetting properties and maintains its jelly consistency at body temperature. It dissolves completely in the vaginal secretions, and possesses the unique property of dissolving large quantities of sulfathiazole which, in turn become soluble in the secretions. This last property makes this jelly far more sulfa active than it is possible to obtain with the usual suspensions of sulfathiazole. The jelly is sterile and can therefore be used as tampons and packs after surgery. The pH approximates 4.0, the buffering power is large, and there is no excessive leakage from the vagina unless the discharge is copious.

This report covers a study of the effectiveness of the above-described sulfathiazole acid jelly in 230 cases of vaginitis and 152 cases of cervicitis. The criteria for cure were: complete relief from symptoms, return to normal pH, and negative smears taken at intervals during the 3 months following termination of treatment. Patients in whom symptoms and laboratory findings indicated more or less complete relief, but who had recurrences before these criteria for cure were completely fulfilled, were designated as improved. Applications of the jelly were made once or twice daily—one application preferably made at night before retiring.

*Vaginitis Cases.* About 83 per cent of the 230 cases of vaginitis were considered cured. Ten per cent were regarded as improved but not cured and in 8 per cent the treatment was ineffective. In general the response to treatment was excellent whether the vaginitis was trichomonal, monilial or nonspecific in origin. Of the 18 failures, 16 were trichomonas and two monilia. In six of these the husband was found to be the cause of continuous reinfection; in two symptoms were controlled as long as the husband used a condom during coitus. Duration of treatment before symptoms cleared completely varied from 1 to 17 weeks and averaged  $5\frac{1}{2}$  weeks. In most cases prompt deodorization of the discharge and elimination of itching were obtained. A change in the type of smear toward the normal and a lowering in pH to the optimal 4.0 to 5.0 were observed

in the improved or cured cases. Repeated determinations of the sulfathiazole level of the blood failed to reveal a demonstrable absorption in any patient.

*Cervicitis Cases.* In the 152 cervicitis cases the sulfathiazole acid jelly was either used alone or as an adjunct to electrosurgical cervical treatment. Nasal-tip cautery was used in 26 cases, conization in 48, coagulation in 44 and no cervical surgery in 34. In all cases the following noteworthy postoperative observations were made:

1. Absence of foul odor.
2. Absence of profuse discharge; during the sloughing period only slight amounts of thin, watery discharge were observed. This usually disappeared following disappearance of the slough.
3. Good control of bleeding; only spotting occurred in 44 cases and slight hemorrhage in 6. These occurred at the time of separation of the slough, usually at about the 12th or 14th day. No subsequent surgery was necessary for their control.
4. A mild stenosis was noted in 6 cases, but pyometra and infection were absent.
5. In all cases the vaginal pH was between 4.0 and 5.0 at the end of treatment.
6. A marked reduction in healing time. In 80 per cent of the cases slough removal occurred within two weeks and healing to full epithelization was complete within 5 weeks in 90 per cent of the cases.

The paper is accompanied by a series of beautiful kodachrome photographs showing the beneficial effects of treatment with the sulfathiazole acid jelly.

(A number of publications have appeared in the past year on the local employment of sulfa drugs for trichomonas vaginitis (See comments on paper by Alexenicer in June Survey, p. 393, and that of Angelucci, February Survey, p. 103). They may be helpful, but I wonder if the evidence for the parasitocidal or fungicidal effectiveness of the sulfa drugs is as good as that for their now established effectiveness against many bacteria.—Ed.)

## FOREIGN BODIES IN THE VAGINA

RANDOLPH H. HOGE

Virginia M. Monthly, 73: 277-280, 1946

The author presents a review of the literature on foreign bodies in the vagina. These have included innumerable and various objects. One vagina contained 2 cherry stones, 2 pebbles, 2 splinters of wood, some scraps of coal and other foreign bodies. A feeble-minded, 23 year old pseudohermaphrodite had on 2 occasions this remarkable collection: a hexagonal-shaped nut, one cm. in diameter, 6 shoe buttons, 2 rubber balls, the cap of a tooth paste tube and a small cork. The author recalls 2 specimens which he believes were in the Harvard Medical School museum, having been removed from vaginas. One was a large Irish potato and the other a ligamentum nuchae of an ox.

The explanation for foreign bodies in the vagina is sometimes obscure. In some cases the placing of an object in the vagina is an act of masturbation; in some it may be due simply to a child's exploratory spirit. Some patients have been mentally deficient. One woman inserted bael fruit to treat a prolapsed uterus. Irate husbands and curious boy playmates have also inserted objects in vaginas.

Leucorrhœa is the outstanding symptom of a vaginal foreign body. A sanguineous discharge in a child is almost pathognomonic of a foreign body. To remove the object, a finger inserted into the rectum can guide the introduction of a probe or hemostat into the vagina in children. The object can be grasped with the instrument under the guidance of the rectal finger, and removed usually without difficulty. In the case of a sharp object, care must be taken not to penetrate the tissues. The use of a urethroscope in the vagina in children may sometimes be helpful.

The author presents 6 cases of foreign vaginal bodies in children. 3 figures.

(In the occasional case, the forcible introduction of foreign bodies into the vagina may cause serious results. Not long ago I removed from the abdomen of a patient a long-handled, glass high-ball muddler or spoon which stretched transversely across the pelvic inlet. Several weeks previously the patient's lover, in a drunken sexual orgy, had playfully thrust it into the patient's vagina, where it penetrated the fornix.—Ed.)

## THE UTERUS

### TREATMENT OF CANCER OF THE CERVIX OF THE UTERUS

GERMAN GARCIA

Ginecologia y Obstetricia de Mexico, 1: 3-24, 1946

Following brief considerations of the well known procedures for diagnosing cancer of the cervix (biopsy, Schiller test, vaginal smear, etc.), the author describes the treatment of this type of carcinoma.

Generally speaking, treatment of carcinoma varies according to the histologic type of the tumor cells and, therefore, to its radiumsensitivity. Since cervical cancer usually belongs to the transitional type and less frequently to the spinal or basal type of cells, it is therefore included within the first group of Borak's classification (cells well differentiated originating from a radiumsensitive matrix) because, excepting the endocervical type of carcinoma, it is made up of well differentiated cells originating from the lining epithelium of the cervix, which is radiosensitive itself. This radiumsensitivity is favored by the solid architecture of the myometrium.

Another important problem to be borne in mind is the question of delimitation of the neoplasm. It is the author's opinion that treatment by irradiations is the best one for carcinoma of the cervix, because even when a radical surgical procedure (Wertheim or Schauta operations) is performed, it is not possible to remove cancer cells from all lymphatics or lymph nodes. Irradiation ought to attack both the cervical tumor and the pelvic cavity at the same time, with doses lethal to the neoplastic elements. This can be accomplished by combining the use of radium and x-ray. The former is directed against the tumor itself and the proximal portions of the parametria, and the latter against its distal portions, situated close to the pelvic wall.

*Radiumtherapy:* The author uses either the Stockholm technique (Heyman) or the Paris technique (Regaud). In the former, however, he only makes one intrauterine application and two intravaginal, with one week interval in between. The vaginal dose varies between 3,000 and 4,500 milligrams hour of element, depending on the surface to be irradiated; the intrauterine dose is 3,500 milligrams hour of element. Intrauterine application of radium is performed under anesthesia, usually of the spinal type. The uterine cavity is then dilated (#13 or 14 Hegar) after which the radium tube is inserted. The latter should fill the whole cavity and be sutured to the anterior lip of the cervix. Vaginal tamponade should be avoided in order to permit good drainage.

On dealing with very infected cases, sulfathiazol or penicillin should be given during the three days prior to the intrauterine application of radium, and continued throughout the latter. Usually the intravaginal application is performed first, followed by the intrauterine one; exceptionally both are done simultaneously.

*X-ray treatment:* Usually two ventral and two dorsal portals are used, measuring 10 x 15 cms. or 10 x 10 cms., according to the size of the pelvis. The lateral portals are never used, since they may be the cause of fractures of the femur. The fractionated method is used with individual doses of 250-300 "r". A dose never less than 2,500 "r" should be administered to each parametrium.

Treatment should always start with radium, not only because it is the main agent in the cure, but also because when x-ray is first used, it may make difficult the further correct application of radium, due to the reaction that it leads to in the vaginal walls. However, x-ray can precede radium whenever large fungoid infected masses are present.

*Complications of radium and x-ray therapy:* Cystitis and rectal tenesmus sequelae can be reduced by using correct dosage and filtration and by placing the applicators correctly. Radiumtherapy should never be started unless a previous cystoscopy has been done. If the bladder already shows cancer lesions, treatment should start with x-ray in order to prevent the possible formation of a fistula. The same plan of treatment is followed for the cancer of the cervical stump.

The author reports a series of 118 cases treated since 1940 by radium and x-ray, apparently cured, although only a few of them have reached the 5-year period following treatment. However, it is interesting to observe that 95.4% of the cases belonged to the advanced groups (II and III) and that 20 of them had already been operated upon without any success.

Concerning the treatment of the vasomotor symptoms resulting from the artificial menopause in these cases, the author avoids the use of estrogens in view of the fact that they might cause an endocrine stimulus in an organism already sensible to a neoplastic growth. On the other hand, since the mechanism of these symptoms is due to a condition of hyperactivity of the pituitary gland as a result of the suppression of the hypophysis-inhibitory effect of the ovaries, it is possible to inhibit the pituitary by using androgens, as many investigators have already reported.

In order to relieve pain in the intractable cases, a solution composed of 2 volumes of methylic alcohol, 1 volume of bi-distilled sterilized water and 1 ctgm. of novocain is administered into the sacral canal. The total amount injected varies from 30 to 40 cc. The analgesic effect has lasted for a period of as much as 5 and 6 months.

(A good review of the radiotherapy of cancer of the cervix, differing in no very important way from that employed in our own clinics. The figures given by the author do not permit of any evaluation of total salvage, but the results reported in the advanced cases which made up the bulk of the author's series are remarkably good. It would be of interest to know his results with earlier cases. They must be good also.—Ed.)

CARCINOMA OF THE CERVIX AFTER  
SUPRAVAGINAL HYSTERECTOMY

W. G. COSBIE

Am. J. Obst. &amp; Gynec., 51: 751-757, 1946

The author discusses a series of 62 patients receiving treatment for carcinoma of the cervix who had previously undergone supravaginal hysterectomy. This series is divided into 2 groups. The first group comprises 24 patients believed to be suffering from carcinoma at the time of operation, and they are referred to as suffering from coincident carcinoma. The second group includes 38 patients, referred to as those suffering from carcinoma of the stump of the cervix.

In the group of 24 patients with carcinoma coincident with supravaginal hysterectomy, failure to investigate the cause of vaginal bleeding accounted for the performance of practically all of the operations. Twenty patients came for treatment within a year of operation, and 15 of these had very advanced tumors which could not have been missed had a preoperative vaginal examination been made. Ten had postmenopausal bleeding, yet even this generally accepted danger signal was neglected. It is concluded that uterine hemorrhage is a symptom of major importance, and the recognition of its cause is essential to avoid the paradox of supravaginal hysterectomy for carcinoma of the cervix.

It is of interest to note that in the entire group of 62 patients there were 9 nulliparous women. Childbirth injury and the consequent development of chronic cervicitis has been strongly emphasized in the etiology of carcinoma of the cervix, but the author considers that carcinoma of the cervix occurs only about twice as frequently in parous as in nulliparous women.

Carcinoma of the cervical stump was diagnosed in the 38 patients at intervals varying from 4 to 36 years after operation. In the author's clinic, cervical stump carcinoma constitutes 4.2 per cent of all cervical carcinoma receiving primary treatment. Total hysterectomy certainly would have prevented the development of carcinoma in these 38 patients, and a review of the case histories suggests that many more total hysterectomies might have been performed without materially increasing the operative risk to the patient.

The results of treatment of the patients suffering from cervical stump carcinoma have been better than the results of treatment of those with carcinoma of the cervix when the body of the uterus was present. The 3-year survival rates were 50 and 39 per cent, respectively, and the 5-year rates were 45 and 30 per cent, respectively. The effectiveness of postoperative irradiation therapy depends on its prompt application.

(This study brings out several points: (1) that panhysterectomy is preferable to the supravaginal technic unless there is some contraindication imposed by the conditions surrounding the individual case or by the personal limitations of the surgeon; (2) that thorough examination of the cervix should be made whenever hysterectomy, or for that matter any pelvic operation, is contemplated; (3) that carcinoma of the stump, when it does occur, and contrary to the earlier view, offers a prognosis no worse than when the body of the uterus is still present.—Ed.)

## CANCER OF THE CERVIX; A NEW TECHNIQUE FOR INTERSTITIAL IMPLANTATION OF RADIUM INTO THE PARAMETRIUM

E. EUGENE COVINGTON

Surg., Gynec. & Obst., 82: 512-517, 1946

The chief purpose of this paper is to show the necessity of interstitial radium therapy for cancer of the cervix and the advantages of a new technique used by the author in 100 cases. It is not a 5-year study, as a few of the patients have been treated for less than 5 years.

Briefly, the technique of radiotherapy was as follows:

1. The first radium treatment consisted of the insertion of 2160 mgm. hours of radium into the intrauterine canal and the packing of 720 mgm. hours of radium as far laterally as possible into either lateral vaginal fornix.

2. Within a few days of the first radium treatment, roentgen therapy was started by which a 42 per cent depth dose was given into the cervix and adjacent parametria.

3. When the roentgen therapy was completed the second treatment or interstitial implantation of radium was done. Four small incisions were made in the vaginal mucosa (not into the parametria) in the 2, 4, 8 and 10 o'clock positions equidistant as far laterally as possible around the cervix. A long Kelly clamp was then used to dissect a long tract into the parametrium through each of the 4 incisions. A rubber tandem containing radium was then inserted into each of the 4 tracts, giving a total of 2520 mgm. hours of interstitial radium. Radium (1680 mgm. hours) was then inserted into the intrauterine canal.

The total irradiation given directly into the tumor was 7800 mgm. hours of radium + 3360 r of roentgen therapy. The author discusses the advantages and contraindications with this new type of interstitial therapy and places emphasis on the greater safety of this procedure over other forms of interstitial therapy.

Of the 100 patients in this series, 76 (76 per cent) are still living and under observation and 24 patients (24 per cent) have died of cancer. The known causes of death were as follows: 3 patients had rectovaginal fistulas, 2 had bone metastases, 2 had pulmonary metastases, 4 died of urinary obstruction, 7 had secondary vaginal hemorrhages and one died of rectal hemorrhage. There were no early complications from the interstitial implantation of radium, but there were 6 cases of irradiation proctitis, one case of rectovaginal fistula and one case of radiation necrosis of the cervix as late complications. The 24 deaths were the results of uncontrolled cancer of the cervix and adjacent parametrium.

From a study of the 5 late complications of irradiation, the causes of death in 24 patients and the high percentage of positive biopsies of lymph nodes of the pelvis found at operation by surgeons, it should be obvious that a higher total dose of irradiation should be given to the cervix and a much higher total dose equally distributed throughout the parametria and lymph nodes of the pelvis.

The author has attempted to accomplish the following: (1) To eliminate the necessity of a major surgical procedure for early carcinoma of the cervix. (2) To improve the complete eradication of the growth in the cervix. There have been fewer positive biopsies after treatment, thus the 5-year cure rate should be better. There have been only 4 deaths (4 per cent) from stage II cancer of the cervix and none from stage I. This rate is far better than was obtained by previous methods of radiotherapy. (3) To reduce the number of deaths from parametrial extension of cancer by giving a higher total dose of irradiation equally distributed throughout the pelvis. This has also been effected as only 4 deaths (4 per cent) were due to urinary obstruction contrasted with the usual 20 to 35 per cent recorded in the literature. 3 figures.

(It is difficult to believe that this rather heroic plan of radium application would not be associated with considerable risk of injury of important structures, especially the ureters. —Ed.)

## IS THE BIOPSY OF NEOPLASMS DANGEROUS?

M. E. MAUN AND W. F. DUNNING

Surg., Gynec. & Obst., 82: 567-572, 1946

There is some experimental evidence to support the belief that the rupture of the capsule of a tumor or the destruction of adjacent tissue structures incurred in obtaining a biopsy specimen may serve to open vascular and lymphatic channels to tumor cells. Therefore, clinicians are prone to avoid the incision of neoplasms for fear that the diagnostic procedures may serve to disseminate tumor cells, but reluctance to perform a biopsy often delays adequate therapy and invalidates an accurate diagnosis.

A critical study of surgical and postmortem specimens gives ample evidence that neoplasms are not restrained or unduly inhibited by their capsules or areas of marked desmoplasia, since metastases may precede capsule formation and emboli may readily flow in lymphatic channels found in encircling tissue barriers. Evidence also suggests that growth in distal parts depends upon the adaptability of the invaded tissues to the repeated attacks of viable emboli. Therefore, it may be supposed that inoculation of an organ with a large mass of tumor cells might produce a viable metastatic focus, while an embolus of only a few cells might succumb to tissue defenses. Hence, a decrease in the bulk of a neoplasm should serve to decrease the incidence of metastatic growth.

Finding that the literature presented contradictory and inconclusive evidence on this subject, the authors thought it desirable to investigate the problem further, employing more biologically uniform material. Rats bearing transplanted fibrosarcoma, adenocarcinoma and squamous cell cancer were operated upon and compared with an unoperated upon control group for length of survival after transplantation and percentage in which metastases were detected.

The average survival period of rats bearing transplanted fibrosarcomas was significantly prolonged by excision of the tumor 9 days after transplantation but the percentage of lung and lymph node metastases was not altered.

The average survival period of rats bearing transplanted adenocarcinoma was significantly prolonged by the removal of a considerable mass of the tumor 60 days after inoculation. The rats operated upon which survived the rats of the control series had a significantly higher percentage of lung metastases.

A simple biopsy performed on rats bearing transplanted adenocarcinoma did not affect the average survival period of the rats or increase the percentage with lymph node and lung metastases.

A simple biopsy of transplanted squamous cell cancer did not affect the average survival period of the rats or increase the percentage of metastasis to the lymph nodes, lungs and skeletons.

These data confirm recent clinical observations that the surgical removal of all available tumor tissue in a seemingly hopeless case serves to prolong the individual's life for several years. Further, no untoward effects are recorded by cutting into the tumor mass or by severing lymphatic channels. These reports and the data reported in the present paper would suggest that the treatment of a neoplasm is facilitated by the removal or destruction of any quantity of the growth and that the hosts' survival is, thereby, proportionately prolonged.

(This interesting experimental study offers evidence (1) that biopsy of malignant tumors is not fraught with danger of disseminating the growth, and (2) that removal or destruction of the primary growth, where dissemination has already occurred, tends to increase the period of survival. This is not the first study of this sort which has been made, nor the first which has led to the conclusions above noted, and yet there have always been surgeons who have felt apprehensive about the risk of spreading cancer cells by the opening of blood vessels and lymphatics which biopsy entails, although there appears to be little or no evidence of worthwhile hazard in this respect from the field of human surgery. In spite of this, the imperfections of our knowledge should induce us to develop gentleness in cancer operations, and to avoid the unnecessary mauling and traumatism which might squeeze cancer cells into the lymphatics or into the peritoneal cavity.

It seems doubtful that vaginal smear studies can ever replace biopsy in the diagnosis of cervical cancer, so that even if there were a slight theoretical hazard to biopsy, we should never hesitate to do it when indicated. In no other way can the diagnosis be absolutely established, and a proper decision on this point is of vital importance to the patient.

As to the second point brought out by the authors, this likewise is in keeping with the experience of most surgeons. For example, in the all too frequent cases of ovarian cancer in which exploration reveals that extensive peritoneal involvement has already occurred, it appears to be true that removal of the primary growth, when this can be carried out without undue hazard, does tend to prolong the patient's life.—Ed.)

# GENERAL PRINCIPLES CONCERNING THE MALIGNANT GRADATION OF CARCINOMAS

MOACYR DE FREITAS AMORIM

Arq. Cir. Clin. Exp. (São Paulo, Brazil), 8: 337-444, 1944

On the basis of a large series of tumors of all types and origins, in which an anatomo-clinic interrelationship had been established whenever possible, the author sets forth a system of grading malignancy of all types of cancer of the various organs, and not only of some varieties, as has been done hitherto.

For this purpose, as a matter of principle, he adopts Broders' numerical system, classifying the grade of malignancy of all carcinomas from I to IV. However, the basic principles guiding his classification differs entirely from Broders' one (previous pseudo-counting of the cells, of the number of mitotic figures, especially of percentage, etc.). As a matter of fact, this classification is based exclusively upon the classical principles of oncology, i.e., the parallelism that exists between the degree of anaplasia or cataplasia of the tumor cells and the grade of malignancy and radiosensitivity of the latter.

Preliminarily, the neoplasm should be classified within a "general" grade of malignancy, by which the grade of malignancy of the neoplasm is compared to all tumors in general. After this has been established, then the so-called "special" grade of malignancy is determined, by which the neoplastic cells on study are related to others of the same variety or group, in order to create the sub-groups or subdivisions. The following table represents the classification recommended by the author:

*Classifying table of the grades of anaplasia and malignancy*

GRADES OF HISTOLOGIC DIFFERENTIATION (OR OF INDIFFERENTIATION AND ANAPLASIA)	GRADES OF MALIGNANCY AND RADIOSENSIBILITY	NUMERICAL GRADATION	GENERAL TYPES OF CARCINOMAS	
			Originating from the surface epithelium	Originating from the glandular epithelium
High grade of differentiation on (or lower degree of undifferentiation or anaplasia)	Low grade of malignancy (and of radiosensitivity)	Grade I	Malignant papillomas	Malignant adenomas
Medium grades of differentiation (or medium grades of anaplasia)	Medium grade of malignancy (and of radiosensitivity)	Grade II	Spinal-cell carcinomas	Adenomatous carcinomas
Low grade of differentiation (or high grade of anaplasia)	High grade of malignancy (and of radiosensitivity)	Grade III	True basal-cell carcinomas (of the mucosas)	Solid glandular carcinomas
Total or almost total absence of differentiation (or maximum grades of anaplasia)	Maximum grade of malignancy (and of radiosensitivity)	Grade IV	Diffuse carcinomas (or meristomas)	

In order to evaluate the malignancy of cancer, the histological grade, although very important and even fundamental, does not, however, suffice if considered alone. Besides the structural characteristics showing a higher or lower degree of anaplasia (histologic malignancy of the tumor), we also have to consider the clinical grade of malignancy, which is obtained by the observation of various important factors: (1) Degree of local extension already acquired by the neoplastic growth. A cancer Grade I, therefore, when very extensive bears a bad prognosis even if its histological malignancy is of low grade. On the other hand, a cancer possessing a high grade of malignancy (II, III or IV) when diagnosed in a very early stage, with a very small local extension, may have a better prognosis, as far as surgery is concerned, and it can even be good or excellent in some instances. (2) The organ involved. A good example is given by the basal cell tumors of the skin, which are relatively benign, while on the other hand, the basal cell carcinoma of the uterine cervix is extremely malignant. (3) The age of the patient. It is known that certain types of cancer are more malignant and show a more rapid course at certain ages than at others. (4) Multiple patterns that can be seen in cases of large neoplasms, leading to mistakes in the interpretation of their histological malignancy, especially when only small fragments of tissue are submitted for pathologic examination.

This article is illustrated with a great number of clinical cases, many of them gynecological ones, accompanied by several photomicrographs.

(The observations upon which the author's system of grading carcinomas is based are sound, but there would seem to be no important difference between his plan and those now in general use. All are based on the belief that the greater the degree of anaplastic activity, or de-differentiation, or unripeness of the constituent cells the greater the degree of clinical malignancy. His system, I am glad to see, classifies as Grade I adenocarcinoma the tumor called by some "malignant adenoma." The author is likewise to be commended for emphasizing that the clinical classification of the tumor, referring to its clinical stage of advancement, is of even greater importance in prognosis than its histologic grading. For example, an advanced carcinoma of Grade I or II presents a more unfavorable outlook than an early lesion of Grade iv.—Ed.)

## OBSERVATIONS ON THE TREATMENT OF ADENOCARCINOMA OF THE UTERUS

L. A. GRAY, M. FRIEDMAN AND W. S. RANDALL

Surg., Gynec. & Obst., 82: 386-404, 1946

The authors present 10 cases of adenocarcinoma of the uterus treated at Walter Reed General Hospital in order to show that residual carcinoma was found in 6 of the 7 uteri which received enormously large doses of radium and to point out the necessity of oöphorectomy as part of the treatment, since ovarian metastasis was present in 3 patients.

It has been suggested that panhysterectomy with bilateral salpingo-oophorectomy should result in a 5-year arrest of 60 to 65 per cent of operable lesions. The majority of recent authors have advocated the use of preoperative radium followed by hysterectomy. Small doses of radium (1500 to 2500 milligram hours) have relatively little effect on adenocarcinoma of the uterus, and the few reported cases treated with 4000 or more milligram hours are inadequate for a correct statistical evaluation of the combined method of therapy.

In the present series of cases radium was applied by means of the hystero-stat, an applicator designed by one of the authors to achieve more equal distribution of radiant energy to all parts of the uterus. The hystero-stat is described and illustrated in the original paper.

Of the 10 cases of adenocarcinoma of the uterus, 9 were moderately advanced or advanced, but without induration of the pelvic ligaments, and were considered operable. Ovarian metastasis was subsequently found in 3 patients. Microscopic examination revealed moderate differentiation (grade 2) in 4 cases, moderate undifferentiation (grade 3) in 4 cases and complete undifferentiation in 2 cases.

Seven of the 10 cases were treated with radium followed by panhysterectomy and bilateral salpingo-oophorectomy, the radium dose ranging from 6030 to 12,480 milligram hours. The single case of adenocarcinoma of the endocervix received an x-ray tumor dose of 3030 r followed by 8000 milligram hours of radium.

The size of the uterus was moderately or greatly reduced following radium. In one case the uterine canal shrank in length from 8 to 4.5 centimeters and in another case from 12.5 to 6.5 centimeters.

The Richardson conservative panhysterectomy technique was used in all but one case. In every case the parametrial tissues were somewhat sclerotic. The uterine vessels seemed smaller than usual. In 6 of the 7 excised uteri nests of apparently viable cancer cells were found in the myometrium, with deeper extension in 3. The one uterus in which no residual carcinoma was found had a highly malignant, undifferentiated adenocarcinoma which received 12,480 milligram hours of radium.

According to the literature, the reasons why combined radium-surgical treatment gives the best results include: (1) reduction of intrauterine infection preoperatively; (2) reduction in size of the uterus simplifying the operative procedure; (3) immobilization of cancer cells in the uterus reducing metastasis; (4) sclerosing of lymphatics and blood vessels, reducing metastasis; (5) prevention of recurrence from operative spill in the vagina and abdominal incision; and (6) favorable results borne out of statistical evidence. However, statistical evidence is the only concrete information on the value of preoperative radium and series of as many as 100 cases with uniform radium treatment (4000 milligram hours or more) will be needed before the value of preoperative radium may be ascertained.

One patient in this series had undifferentiated adenocarcinoma for which many authors recommend preoperative radium. Since the evidence indicated an early

lesion, hysterectomy was performed without preliminary radium. The finding of ovarian metastasis in 3 patients emphasizes the importance of postradium operation, since preoperative radium cannot materially affect the metastatic ovarian lesion.

From this study the authors conclude that radium alone will not completely eradicate adenocarcinoma of the uterus. Subsequent excision of uterus, tubes and ovaries is necessary. The exact rôle and specific indications for preoperative radium therapy have not yet been satisfactorily established. 36 figures.

(This excellent study has yielded results quite similar to that reported from the analysis of a somewhat larger group of cases by Stowe (*Am. J. Obst. & Gynec.*, 51: 57, 1946—abstracted in *June Survey*, p. 406). The popular treatment of the day for adenocarcinoma is preliminary intrauterine radium followed, usually about 6 weeks later, by panhysterectomy and bilateral salpingo-oophorectomy. As the authors point out, however, it is still too early to evaluate the final results of this plan, and not all gynecologists are fully committed to it. For example, in a paper before the recent meeting of the American Gynecological Society, and as yet unpublished, Norman Miller advocated the preliminary use of x-ray alone, with no intrauterine radium. The evidence is piling up that intrauterine radium therapy has many shortcomings, and that residual carcinoma is to be expected in a very large proportion of cases. The one thing which is clearly established is that, unless there is some important contraindication, panhysterectomy should always be a part of the treatment of corporeal adenocarcinoma.—Ed.)

## CARCINOMA OF THE FUNDUS UTERI

ROBERT J. CROSSEN

South. M. J., 39: 445-453, 1946

The author discusses the etiology, diagnosis, classification, treatment and prevention of carcinoma of the endometrium.

Age plays an important rôle in the etiology of endometrial carcinoma; it is seldom seen before 45 and is most common in the 5th decade of life. Another etiological factor concerns estrogen. Certain investigators have been able to produce hyperplasia of the endometrium in castrated animals by prolonged administration of estrogenic hormones. Many workers now feel that hyperplasia may be a predisposing factor in the development of endometrial carcinoma. The absence of the corpora lutea, with its inhibiting effect on the carcinogenic action of estrogens, also probably is a factor in late menopause cases.

In regard to diagnosis, there are the suggestive signs and symptoms and the conclusive pathologic diagnosis. The most frequent symptoms are recurrence of bleeding 6 months to a year after the menopause, and delayed menopause. The indiscriminate use of large doses of estrogenic substances during the menopause, with its accompanying episodes of withdrawal bleeding, may confuse the picture, and in case of uncertainty all estrogenic therapy should be stopped so as to rule out this bleeding factor. The positive diagnosis of adenocarcinoma of the

endometrium is made by careful curettage. The curettage must be thorough, covering the entire surface of the cavity. In cases of recurrent bleeding or persistent discharge after a negative curettage, the curettage should be repeated. As an accessory or preliminary method of diagnosis, the vaginal smear may prove helpful.

The author believes that if a practical classification such as that of H.S. Crossen were applied by surgeons generally and the results recorded, much would be added to our knowledge of prognosis in corpus cancer. H. S. Crossen's classification of endometrial carcinoma is pictorially illustrated in the present paper, and may be stated as follows:

First Stage—endometrium only involved.

Second Stage—myometrium involved but not beyond the middle.

Third Stage—myometrium involved extensively (beyond middle).

Fourth Stage—involvement of removable adjacent structures.

Fifth Stage, (1) involvement of irremovable structures, but primary tumor mass still removable, and (2) involvement of surrounding structures to such an extent as to preclude even palliative removal of the main tumor mass.

The treatment of endometrial or corpus cancer has shifted from radical removal of the pelvic structures to a plan consisting of preoperative radiation, operative removal, and postoperative x-ray treatment. Unless there is some serious contraindication, every patient with fundal carcinoma should be given the benefit of exploratory operation before being considered inoperable from a technical standpoint. The author discusses the problem of distributing the intra-uterine radium.

In regard to prophylaxis against adenocarcinoma of the endometrium, it is felt that it is better to stop the persistent estrogenic activity causing delayed menopause at about the age of 50 rather than run the risk of continued endometrial stimulation. This can easily be done with a radium treatment. Persistent hyperplasia, even in younger women, should be watched carefully and estrogenic therapy avoided. Menopausal symptoms are usually controlled by thyroid, if needed, and small doses of stilbestrol or true estrogens; hence, the practice of giving large doses of estrogenic substances to menopausal patients is not indicated, and may be harmful. 7 figures.

(This is a very good paper, embodying sound views as to the clinical characteristics, pathological diagnosis and treatment of corporeal carcinoma. I agree with the author as to the not infrequent significance of a late menopause in the subsequent development of adenocarcinoma, and as to the possible predisposing role of postmenopausal hyperplasia. As a matter of fact, these two factors are closely related with each other. Crossen speaks of the frequency with which adenocarcinoma is seen in the immediately postmenopausal years, but the significance of this is not always the same. It is at this age particularly that one is most likely to see various proliferative and adenomatous types of hyperplasia, totally different in appearance from the common Swiss-cheese type, and often incorrectly diagnosed as adenocarcinoma.

The safe differentiation of these endometrial pseudomalignant conditions from actual cancer requires large pathological experience, and in a certain proportion there will still be some doubt. In such cases the proper treatment should be that of adenocarcinoma, with usually good results. There is no doubt, however, that many errors are made, with of

course some vitiation of adenocarcinoma statistics. In the even markedly proliferative but benign cases, my experience has been that proper radiotherapy is all that is required for permanent cure, as with the ordinary cases of functional bleeding.

I do not believe that the classification of H. S. Crossen for endometrial carcinoma will be as valuable for prognostic purposes as his son believes, chiefly because it is apparently based almost entirely on the degree of myometrial penetration, based usually on the study of a few scattered sections. An adenocarcinoma which may be quite advanced, with poor prognosis, sometimes shows surprisingly little or no myometrial penetration, while in other lesions an adenocarcinoma involving only a very limited endometrial area may show deep myometrial penetration, even to the peritoneum.—Ed.)

## SOME ASPECTS OF CANCER OF THE ENDOMETRIUM—ITS ASSOCIATION WITH PREGNANCY

OSCAR B. NESTAREZ AND NICOLAU S. ASSALI (São Paulo, Brazil)

*Obstetricia y Ginecologia Latino-Americanas* 4: 161-189, 1946

On the basis of three cases, one of epidermoid cancer of the endometrium associated with uterine pregnancy and removed by curettage, one of squamous metaplasia of the endometrium with beginning malignant degeneration, and another of polypoid hyperplasia showing a malignant tendency, the authors discuss the incidence of cancer of the body of the uterus, its etiopathogenesis, the question of precancer, the incidence of epidermoid carcinoma "per se", as well as of carcinoma of the endometrium associated with pregnancy and its cure by means of curettage.

According to the authors, multiparity does not seem to influence the incidence of endometrial carcinoma, nor do abortions.

There is no relation of cause and effect between myoma and corporeal carcinoma, although they might frequently coexist, nor does the presence of the former aggravate the operative mortality of the latter.

Hyperplasia of the endometrium and cancer of the body of the uterus are closely related within or beyond the menopause, because (1) post-menopausal hyperplasia is probably caused by estrogenic activity, which has been encountered by many investigators in some cases of endometrial carcinoma; (2) sometimes it is very difficult for the pathologist to distinguish what is hyperplasia from what is carcinoma; (3) several investigators have been able to trace the transition of one process into another; and also hyperplasia of the basal layer of the endometrium may lead to carcinoma.

The question of precancer is exclusively of clinical nature, although in some instances it has a pathological basis. As a matter of fact, there are conditions and lesions of the endometrium that can become malignant, whenever special general stimuli, hormonal or not, and particular individual conditions participate also: squamous metaplasia, endometrial hyperplasia, mucous glandular polyp, benign adenoma, papilloma and chronic inflammation.

Regarding epidermoid carcinoma of the endometrium, it must be said that it is a very rare disease and has to be distinguished from the so-called adenoacanthoma. In order to explain its histogenesis, the best concept is offered by the indirect metaplasia (Krompecher) theory.

Carcinoma of the body of the uterus coexisting with uterine pregnancy constitutes a very rare eventuality, and even more rare when the carcinoma is of the epidermoid type, as in one of the author's cases, which constitutes the eighth reported in the whole literature.

The cure of endometrial carcinoma by simple curettage has already been described by some authors, and can be explained by assuming the fact that in the early stages, the tumor may sometimes remain localized in a small area, and, therefore, a thorough curettage may remove it entirely.

*Case reports:* 1) 40-year-old patient who had become pregnant 4 months ago. Following a period of amenorrhea of one month and twenty days, she started bleeding. Two curettages were performed, but did not control the metrorrhagia. Pelvic examination was negative. With a diagnosis of incomplete abortion, the patient was submitted to a third curettage, at which a soft zone could be felt on the right side of the fundus, leading to the suspicion of malignancy. Pathological examination of the curettings revealed infected ovular rests and an epidermoid carcinoma of the endometrium (grade III).

Total hysterectomy and bilateral salpingo-oophorectomy were performed, followed by uneventful recovery. Pathological examination of the surgical specimens revealed only chronic endometritis, no malignant cells being seen.

This case, therefore, constitutes a good example of real cure of an endometrial carcinoma following a simple curettage.

*2nd Case:* This concerns a case of squamous metaplasia of the endometrium with beginning malignant degeneration. A 36-year-old patient complained of vaginal bleeding for 30 days. Her history could not be obtained, due to lack of knowledge of the language. Pelvic examination was negative. With a clinical diagnosis of functional bleeding or abortion rests, a curettage was performed. Pathological examination of the scrapings revealed carcinoma of the endometrium.

Total hysterectomy and right salpingo-oophorectomy were done, followed by uneventful recovery. Pathological examination of the organs removed showed only chronic cervicitis, chronic endometritis and squamous metaplasia of the epithelium lining the glands.

*3rd Case:* This concerns a case of polypoid hyperplasia with malignant tendency. A 52-year-old patient in menopause for the last 5 years, complained of vaginal bleeding during the last 3 months. Pelvic examination was negative. A curettage was performed, which showed polypoid hyperplasia of the endometrium with signs of malignant degeneration. There were numerous irregular glands lined by epithelium showing no uniform distribution. In the compact layer there were many epithelial proliferations growing in an infiltrating form, in the midst of a compact connective-muscle tissue.

This patient was submitted to radium therapy and is fairly well up to today.

(The authors' discussion and case reports open up many important questions, only one or two of which can be commented upon. They speak of the now large group of cases in the literature in which curettage has cured adenocarcinoma, but it must be remembered that in all these the curettage has been followed by hysterectomy, the latter probably being responsible for the cure. In such cases the curettage removes a small localized, usually polypoid adenocarcinoma, so that no evidence of cancer can be seen in the uterus after its removal. But this does not necessarily mean that if nothing more than the curettage were done, the patient would remain well. Such an assumption would not be in conformity with our usual ideas of cancer characteristics.)

As the illustrations are not especially good, it is difficult to be sure of the authenticity of the diagnosis in Cases 1 and 2. As regards Case 1, it should be borne in mind that plaques of decidual cells might in some cases be readily confused with epidermoid carcinoma. Case 3 was evidently one of proliferative but benign hyperplasia. While the ordinary Swiss-cheese hyperplasia does not in any way resemble carcinoma, the occasional case with markedly proliferative and adenomatous features may offer great difficulties, so that pathologists will disagree as to the diagnosis. This pseudomalignant variety of hyperplasia, in my experience, is most likely to be seen in women over 50. There are cases in which the pathologist, if experienced in this field, must at times make a diagnosis based almost on instinct and empiricism. If he is in serious doubt, hysterectomy is advisable, but in this doubtful group my experience has been that examination of the removed uterus is likely to show no carcinoma, though there are of course exceptions.—Ed.)

## CHRONIC INVERSION OF THE UTERUS WITH FIBROSARCOMA OF THE CORPUS

W. J. REICH AND M. J. NECHTOW

Am. J. Surg., 71: 710-712, 1946

While sarcoma of the uterus may arise from the muscle fiber of the uterus, the connective tissue, or the endometrium, the commonest source is fibromyomas of the uterus. The incidence of sarcomatous degeneration of fibromyomas is probably .5 to 1 per cent, although some clinicians have found it as high as 4 per cent. Sarcomas originating from fibromyomas are thought to bear a much brighter prognosis than primary sarcomas. It is also believed that the degree of mitotic activity may reflect the severity of the malignancy and its clinical prognosis.

Non-puerperal uterine inversions are usually caused by some sort of neoplasms of the fundus. Fibromyomas are the commonest tumors associated with a non-puerperal inversion. The author presents the case of a 76 year old woman in whom, on examination, a large necrotic mass protruded from the vagina. To the right of this mass there was an adherent decomposed necrotic tumor measuring 4 by 4 cm., the center of which appeared "cooked", while the periphery was yellowish green. It was friable and bled easily. The entire protruding mass was markedly edematous and it was impossible to reduce it back into the vagina. A preoperative diagnosis of chronic uterine inversion, accompanied by a degenera-

ating fibromyomas, was made; malignancy was considered probable. Vaginal hysterectomy was performed and histologic sections proved it to be a fibrosarcoma. 3 figures.

## VAGINAL AND CERVICAL CYTOLOGY IN UTERINE CANCER DIAGNOSIS

J. ERNEST AYRE

Am. J. Obst. & Gynec., 51: 743-750, 1946

This paper consists of an analysis of 100 cases of genital malignancy studied in the Gynecologic Cytology Division of the Royal Victoria Hospital. Of these 100 cases giving a tissue diagnosis of malignancy, the cytology smears showed an average error of 6 per cent. Results are outlined in Table II.

TABLE II

### Results

Total number of cases investigated (patients of cancer age or with cancer signs or symptoms).....	580
Smears diagnosed positive for cancer.....	105
Smears diagnosed negative for cancer.....	475
Number with positive smears having positive biopsy.....	96
Number with positive or suspicious smears having negative biopsy (percentage of error—8).....	9
Number with negative smears having positive biopsy (percentage of error—4).....	4

Smears taken routinely from the external cervical os have been found more reliable in diagnosis than vaginal smears. Smears taken direct from the cervical os gave a more rapid and efficient identification of the malignant cells. The author states that this would seem the more logical procedure because over four-fifths of the genital malignancies do arise from the cervix or from the endometrium.

It is pointed out that the cytology of the cervical canal is different from that in the vagina. In malignant cases one finds fewer of the normal squamous epithelial cells and a greater quantity of mucus and leucocytes, and more significant, a greater concentration of malignant cells. Because the cervical smears exhibited a greater concentration of cancer cells, it was found advisable to modify the original technique of Papanicolaou and Traut.

It has been the author's experience that a diagnosis of malignancy of the endometrium can be reliably determined by the smear method, but there is a slightly greater risk of error in this type than in cervical malignancy. Exfoliation from the endometrium occurs abnormally in the presence of any degenerating, necrosing

or bleeding lesion. Another factor that accounts for the greater percentage of error in the cytology diagnosis of fundal malignancy is the fact that so many lesions occur which are on the borderline between extreme endometrial hyperplasia and adenocarcinoma.

Advantages of cytology diagnosis are that it often completely eliminates the danger of added trauma, bleeding and lymphatic extension of the cancerous lesion, and that, in the presence of sepsis contraindicating surgical biopsy, smears may be taken without stirring up the infection. The smear is also helpful in differential diagnosis of lesions in patients known to have a positive Wassermann test. Also, the increased economy of the smear method over biopsy may not be overlooked.

The author has found that the centrifuge cytology technique offers several advantages over the smear. By gathering up the sediments from the bottom of the bottle, it was realized that this sediment contained in it the telltale cancer cells which when placed in a corked test tube in a few drops of fixative solution could be at once fixed and preserved and then easily mailed. As many of the cervical aspirations were rich in blood and secretion, the specimen was centrifuged, then mounted in paraffin, sectioned, and stained with hematoxylin and eosin. Using this technique, the cancer cells may be more quickly identified, being thrown together by the centrifuge. Staining is simplified as ordinary hematoxylin and eosin usually is satisfactory for routine use.

In conclusion, the author states that the smear method has been helpful in detecting cancer at an early stage and in benign cases simulating malignancy clinically. The method has also been found valuable in assessing radiation therapy. 3 plates.

(The question of vaginal cytology in the diagnosis of uterine cancer has already been commented upon rather fully in recent issues of the Survey (February, p. 106; April, p. 255) so that it need not be again discussed here. Ayre makes the suggestion in his paper that the smears be taken routinely from the external cervical os instead of from the vagina, and this seems logical, at least as applied to endometrial or intracervical cancer. Theoretically, however, this method might miss the occasional lesion just outside the os. Without again reiterating the pros and cons of the vaginal smear method, the prevailing opinion, even among those who have used it most widely, is that it can not take the place of biopsy in the decisive diagnosis of cancer, but that it may develop into a valuable screening test in the examination of large numbers of women.—Ed.)

## CERVICAL CYTOLOGY TESTS IN CANCER DIAGNOSIS: GLYCERINE TECHNIQUE FOR MAILING

J. E. AYRE AND EVELYN DAKIN

Canad. M. A. J., 54: 489-491, 1946

The authors describe a new cytology technique whereby vaginal and cervical smears may be temporarily mounted for mailing by the glycerine technique.

The cancer cells and normal cells lose none of their morphological interpretation of cancer or pre-cancer. The instructions for the glycerine technique are as follows:

1. A glass pipette is used to aspirate the secretion from the external cervical os. The secretion is spread over a  $\frac{3}{4}$  inch diameter area at one end of the slide. The smear is immediately immersed in the solution containing equal parts of 95% alcohol and ether, and the slide is allowed to remain immersed for one hour.

2. At the end of one hour the slide is removed and, without permitting drying, a large drop of glycerine is placed in the center of the secretion zone. A second glass slide is placed face to face with the smear and the glycerine spreads out to cover the entire smear area, sealing it off completely. The 2 slides are then placed in a tiny wooden container for mailing to the laboratory. They may remain in the temporary glycerine mounting up to 2 weeks, if necessary, but the best staining results will be obtained if the time does not exceed one week.

3. The staining procedure is carried out in the cytology laboratory. The cover slide is removed by rotating one slide on the other slightly preceding separation. The slide containing the cell smear is placed in absolute alcohol for 5 minutes to allow the glycerine to dissolve, and then is stained as follows:

a—Wash in 70, then 50% alcohols; then rinse well in 2 changes of distilled water.

b—Stain in Harris hematoxylin for 6 to 10 minutes.

c—Rinse thoroughly 3 to 4 times in 0.5% aqueous solution HCL.

d—Rinse thoroughly in running tap water 10 to 15 minutes.

e—Rinse in 50%, 70%, 80%, and 2 changes of 95% alcohol (do not carry any water into OG-6).

f—Stain for one minute in OG-6, depending on age of stain.

g—Rinse 5 to 10 times in each of 2 jars of absolute alcohol to remove excess stain.

h—Stain in EA-50  $2\frac{1}{2}$  to  $3\frac{1}{2}$  minutes.

i—Rinse 5 to 10 times in each of 3 jars of 95% fresh alcohol.

j—Rinse in absolute alcohol.

k—Rinse in zylol (1) and (2), allowing to stand a couple of minutes in second zylol before mounting.

l—Mount in Canada balsam or permount.

By using this technique, the cytology test for cancer becomes as readily available to the physician's use as a Wassermann test. 1 figure.

(As discussed in a number of previous editorial comments on papers dealing with the vaginal smear diagnosis of uterine cancer, one of the limitations of the method is that an expert knowledge of vaginal cytology is requisite for trustworthy interpretation. The method of collection and preliminary preparation of the smears which the authors outline should be of help, since it leaves the staining and, above all, the cytological diagnosis to those qualified in this field.—Ed.)

## LYMPHANGIOCYSTIC FIBROMA OF UTERUS

ALFRED PLAUT

Am. J. Obst. &amp; Gynec., 51: 842-851, 1946

The case report presented in this paper is the twenty-first case of lymphangiocystic fibroma of the uterus reported.

The patient was a 50 year old gravida iv, para iv, complaining of irregular periods for one year, the menstrual intervals during this time having varied from 3 weeks to 3 to 4 months. During the past few months prior to admission there had been intermenstrual spotting, weakness and backache. The past history was irrelevant. Physical examination revealed heart and lungs normal, abdomen soft, no masses felt, no pain elicited. Vaginal examination revealed a slight rectocele and hypertrophied cervix. A firm mass, about 2 cm. in diameter, protruded from the external os; it had a pedicle which appeared to lead into the uterine cavity. The uterus was retroverted, about the size of a 6 weeks' gestation and its posterior wall appeared irregular, hard and nodular. The appendages were negative.

A preoperative diagnosis of "submucous uterine myoma" was made and vaginal hysterectomy and perineorrhaphy were performed under spinal anesthesia. The pedicle of the mass protruding from the external os was found to be attached to the posterior cervical lip, a short distance above the external os. The small tumor grossly was found to be round, ovoid and partly cystic. The patient's recovery was uneventful.

No myomas were found in the uterus. The endometrium was thick, partly yellowish, partly red. The myometrium was up to 2.5 cm. thick. The cervical lips were everted, funnel-like. The tumor mass was pinkish-gray, soft, cystic and ovoid, its largest diameter measuring 3 cm. Its inside was glossy, purplish pink with irregular small, flat ovoid protrusions.

The tumor was separated by a layer of normal cervical stroma from a zone of severe cervicitis; in no place did the inflammation reach the tumor. Microscopically no capsule was found. Finger-shaped portions of tumor and normal tissue interlocked. Slight loosening of texture was the only indication of histolysis. The tumor represented a shell surrounding a ragged central cavity, which in turn was surrounded by a system of clefts. Most of these clefts apparently did not communicate with each other. Some were empty, while others were filled with thin, homogeneous matter or "fuzzy" coagulum. In most places, no lining layer was seen; at some points a single layer of flat cells lined the cavity. Gross sections of blood capillaries protruded from the nonlined inner surfaces; however, no hemorrhage was seen anywhere in the tumor. Small areas of liquefaction were numerous, notably around blood and lymph vessels. Vessels were very numerous, most of them were sinusoidal capillaries or venules. There were blood vessels, lymph vessels and endothelium-lined spaces whose nature was doubtful.

An even network of collagenous bundles occupied the tumor. A lymph node had been beginning to form in the tumor. No elastic fibers were found, and no muscle fibers. Cells were evenly distributed; there were neither heaps, bundles nor whorls. No cell boundaries could be recognized. The nuclei were more or less oval, on the average 6 to 9 microns long, the distance between them averaging 8 to 10 microns. A single medium-sized nucleolus was seen in many cells. Occasionally, 3 to 5 nuclei were close together, but there were no giant cells. No cell division was found.

Single, small, compact round, probably lymphocytic, nuclei were sparsely scattered. In the areas of liquefaction, slightly larger dark nuclei were found in groups, and around some a narrow zone of cytoplasm could be recognized. One single cell had small indistinctly eosinophilic granules. Tissue mast cells were numerous. The anatomic diagnosis was hyperplasia of myometrium, small lymphangiocysto-fibroma, cervicitis.

It appears that the typical lymphangiocystic fibroma is benign; however, sufficient follow-up data are lacking. The author discusses questions of diagnosis and procedure. 9 figures.

(This is an extremely rare uterine tumor, but, as the author suggests, perhaps not quite so rare as the literature would indicate. For example, I have recently studied two cases of this general group in our laboratory, though both were of solid type, with no such cystic cavity as Plaut describes in his specimen. I wonder why he calls it a lymphangiocystic fibroma, rather than simply a lymphangioma, since fibroma is practically never seen in the uterus, and the illustrations show little evidence of fibrous tissue. There would be somewhat more reason for his designation as applied to certain equally rare tumors of the ovary, in which even large cystic cavities may show a wall of lymphangiomatous tissue quite similar to that shown in Plaut's pictures. I have recently encountered such a case.

In the uterine group, it is not always easy to draw the line between lymphangioma and lymphangioendothelioma. In one of my own cases, for example, there are areas in which the endothelium shows marked proliferation and apparently some invasiveness, and microscopically one would be inclined to assume at least a low grade of malignancy.—Ed.)

## THE SYMPTOMATOLOGY OF UTERINE RETRODISPLACEMENTS

CLARENCE C. BRISCOE

Pennsylvania M. J., 49: 739-741, 1946

The symptomatology of retrodisplacements of the uterus has been a controversial problem. The idea that this condition is a common cause of abortion and a factor in sterility appears to be rather prevalent. The present paper is based on a review of the records of 500 unselected, consecutive private patients, and represents an attempt to determine if the common impressions about retrodisplacements are based on fact or mere prejudice.

About  $\frac{1}{4}$  of normal healthy women have uterine retrodisplacements. The incidence of abortion of all types is probably 20 to 25 per cent of all pregnancies.

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The patient was a 50 year old gravida iv, para iv, complaining of irregular periods for one year, the menstrual intervals during this time having varied from 3 weeks to 3 to 4 months. During the past few months prior to admission there had been intermenstrual spotting, weakness and backache. The past history was irrelevant. Physical examination revealed heart and lungs normal, abdomen soft, no masses felt, no pain elicited. Vaginal examination revealed a slight rectocele and hypertrophied cervix. A firm mass, about 2 cm. in diameter, protruded from the external os; it had a pedicle which appeared to lead into the uterine cavity. The uterus was retroverted, about the size of a 6 weeks' gestation and its posterior wall appeared irregular, hard and nodular. The appendages were negative.

A preoperative diagnosis of "submucous uterine myoma" was made and vaginal hysterectomy and perineorrhaphy were performed under spinal anesthesia. The pedicle of the mass protruding from the external os was found to be attached to the posterior cervical lip, a short distance above the external os. The small tumor grossly was found to be round, ovoid and partly cystic. The patient's recovery was uneventful.

No myomas were found in the uterus. The endometrium was thick, partly yellowish, partly red. The myometrium was up to 2.5 cm. thick. The cervical lips were everted, funnel-like. The tumor mass was pinkish-gray, soft, cystic and ovoid, its largest diameter measuring 3 cm. Its inside was glossy, purplish pink with irregular small, flat ovoid protrusions.

The tumor was separated by a layer of normal cervical stroma from a zone of severe cervicitis; in no place did the inflammation reach the tumor. Microscopically no capsule was found. Finger-shaped portions of tumor and normal tissue interlocked. Slight loosening of texture was the only indication of histolysis. The tumor represented a shell surrounding a ragged central cavity, which in turn was surrounded by a system of clefts. Most of these clefts apparently did not communicate with each other. Some were empty, while others were filled with thin, homogeneous matter or "fuzzy" coagulum. In most places, no lining layer was seen; at some points a single layer of flat cells lined the cavity. Gross sections of blood capillaries protruded from the nonlined inner surfaces; however, no hemorrhage was seen anywhere in the tumor. Small areas of liquefaction were numerous, notably around blood and lymph vessels. Vessels were very numerous, most of them were sinusoidal capillaries or venules. There were blood vessels, lymph vessels and endothelium-lined spaces whose nature was doubtful.

Many of the animals were pretreated with stilbestrol to increase the irritability of the uterus.

In unanesthetized dogs and rabbits uterine pressures and action potentials were recorded optically from an intra-uterine balloon and silver chloride coated electrodes. Ephedrine, Trasentin, Pavatrine, morphine, beta-diethylaminoethyl phenyl-alpha-thienylglycolate hydrochloride (Stearns 600), beta-diethylaminoethyl phenyl-alpha-thienyl-acetate hydrochloride (Stearns 606), Priscol and magnesium sulfate were evaluated as uterine antispasmodic agents.

Many of these drugs were evaluated by the uterine bath method substituting pitressin or uterine stretch as a measure of inducing activity.

The incidence of spontaneous abortion, according to collective authorities, is 10 per cent. In 100 unselected abortions, the author found only 7 women with retrodisplacements. On the contrary, of 35 patients with retrodisplacements in early pregnancy, only one aborted. Almost all of these retrodisplaced uteri were found at the 6th or 8th week of gestation. The further advanced the pregnancy at the time of examination, the fewer retrodisplacements are found, thus showing that the condition usually corrects itself spontaneously. Findings similar to the author's have been made by Huntington who found a normal incidence of retrodisplacement among 28 women who aborted 68 times. In the event of incarceration, abortion or other dire consequences may result, but considering the number of women with displacements who become pregnant, the reported incidence of incarceration is indeed insignificant.

In regard to sterility as a result of retrodisplacement of the uterus, of 43 infertile patients, only 4 (9.3 per cent) had retrodisplacements. Other workers have reported 4 and 5.2 per cent, respectively, as the incidence of retrodisplacement among infertile patients.

Only 11 per cent of the author's patients with dysmenorrhea had retrodisplacements. Stacey remarks that only 16 per cent of 202 women with retrodisplacements complained of cramps. Suspensions or pessaries will not cure dysmenorrhea.

Of 41 patients whose chief complaint was backache, 8 (19 per cent) had retrodisplacements, while of 80 women with retrodisplacements only 10 per cent had backache.

The author questions: "Why not just admit and teach that uncomplicated retrodisplacements are of no clinical importance?" As Miller says, retrodisplacements cause no symptoms unless the pelvic diaphragm and pelvic floor are injured.

(The author's findings in this interesting study lead him to conclusions which have long guided the practice of all conservative gynecologists. A woman can be just as healthy and happy carrying her uterus posteriorly as anteriorly. There are of course still certain cases which require correction, as when the uterus is large, boggy and subinvolved as well as retroflexed, and when careful study convinces the gynecologist that the displacement is the cause of the patient's symptoms. But the many types of suspension operations formerly so abused are now done far less frequently in all good clinics, and are certainly never to be advised for the numerous cases of symptomless congenital retrodisplacement.—Ed.)

## EVALUATION OF UTERINE ANTISPASMODICS

R. A. HUGGINS AND R. A. WOODBURY

Federation Proc., 5: 183, 1946

Accepted and proposed uterine antispasmodics were tested in animals where uterine activity was induced by pitressin and distention or stretch of the uterus.

formation in the gonads, when a complete anatomical differentiation has not yet taken place. Finally the tumor would show a folliculoid pattern, which corresponds to the structure presented by the gonads already differentiated. As an index of maximum differentiation, the cells would show an epithelial pattern, giving rise to the luteinized granulosa cell tumors sometimes coexisting with a differentiated structure proper of the thecomas.

*2nd Group: Arrhenoblastomas.* As the preceeding group, these tumors seem to originate from an undifferentiated mesenchymatous nucleus, because of the following reasons: 1) Existence of an undifferentiated structure with mesenchymatous character within the group designated by Robert Meyer as atypical; 2) Polymorphism in its constitution; 3) Resemblance of the structure of these tumors to that presented by the gonad in its different stages of development; 4) In the more differentiated forms, the arrhenoblastomas assume an epithelial character; 5) Hormonal activity is observed in those forms presenting cells of epithelial character with the protoplasm loaded with lipoids, which Schiller identifies as the interstitial cells of the testicle. 6) In order to explain why the "adenomas tubulares of Pick" do not exhibit hormonal activity, Schiller supposes that the canalicular portions do not correspond to the seminiferous ducts of the normal testicle. According to their type of epithelium and arrangement, they seem more likely to be related to the "rete" testicular than to the seminiferous ducts, where normally is localized the testicular secretion. Therefore, only the tumors in which parenchyma has differentiated in order to form seminiferous canaliculi would show hormonal activity. On the other hand, those tumors in which differentiation has been carried out the formation of "rete testis", do not exhibit hormonal activity.

In order to explain the development of such special ovarian tumors, the author accepts the view extended by Goldschmidt and Moskowicz, by which every individual is bisexual, the sex being determined by the predominance of either the male or female factors. Therefore, the feminizing tumors would arise when there would be a predominance of the feminizing factors. On the other hand, if the masculinizing factors are predominating at the time, an arrhenoblastoma would be likely to develop. And if there is no predominance of either factor whatsoever, a dysgerminoma would constitute the growth.

(This paper sums up quite satisfactorily our present day concepts of these tumors. The evidence as to the origin of granulosa cell and thecomatous tumors from the progranulosa and prothecal ovarian mesenchyme is now quite strong. As to the masculinizing tumors, there is still considerable confusion. The original explanation offered by Meyer, that arrhenoblastoma arises from vestiges of male-directed cells persisting in the ovarian medulla, does not seem to be adequate, and other factors, including probably some unknown link-up with the adrenal cortex, are probably concerned. There is also confusion as to the few so-called masculinizing luteomas which have been reported, and as to whether they are not really of adrenal cortical origin. There are many points of similarity between adrenal and lutein tissue, not only histological but also functional. For example, the normal adrenal cortex is now known to produce not only estrogen but also a progesterone-like hormone. It is in this still shadowy relationship between the two glands that we may expect future help in the explanation of the origin and histological characteristics of the masculinizing tumors of the ovary.—Ed.)

## THE ADNEXA

### HISTOGENETIC CONCEPT OF THE OVARIAN TUMORS WITH HORMONAL ACTIVITY

EMILIO GIL VERNET

Toko-Ginecologia Practica (Madrid, Spain), 5: 114-125, 1926

The author discusses the different theories proposed to explain the histogenesis of this interesting group of tumors, supporting the later one proposed by Schiller and Novak.

*1st Group: Feminizing tumors* (granulosa cell tumor and thecoma). According to Schiller and Novak's ideas, these tumors arise from a nucleus of undifferentiated mesenchyma, just as the normal granulosa cells proceed from differentiation of the mesenchyma (Fischel). This theory has the following supports: 1) Resemblance, more or less marked, of the histology of these tumors with that presented by the ovary in different stages of development; 2) Polymorphous picture presented by these tumors, and in some, a transition of one type into another; 3) Differentiation and maturity. Although in a given tumor its elements may show different patterns, their degree of differentiation and maturity is however the same. Thus, in some areas there may be trabeculated cells while in others a folliculoid pattern may be seen, but their cells are characterized by undifferentiation. On the other hand, there are cases in which certain portions of the tumor present an epithelial pattern and others show differentiated connective tissue elements, with the structure proper of the thecomas alternating with others of pure fibromatous aspect. However, they all have in common a high degree of differentiation and maturity. The author has not as yet been able to observe the coexistence of the highly differentiated and undifferentiated forms, the latter designated by Robert Meyer as sarcomas. 4) According to their different structural elements, these tumors show an evolution resembling the one presented by the normal granulosa cells. As a matter of fact, the so-called luteomas appear to represent a functional maturity or a stage of complete development or differentiation of the granulosa cell tumors. 5) Identical hormonal activity of granulosa cell tumors and thecoma, i.e., high estrogenic activity, which can be explained by their common origin from a mesenchymatous nucleus. Therefore they exhibit identical biological activity, despite their pathological pictures being distinct.

According to their evolution, these tumors would first appear as undifferentiated elements presenting a mesenchymatous character, which would correspond to the early stage of gonadal development. Afterward the cells would arrange themselves in order to form trabecules or cords, although in a still undifferentiated character. Here the tumor could be mistaken for an arrhenoblastoma of the atypical type. This stage corresponds to the one of sexual cords

formation in the gonads, when a complete anatomical differentiation has not yet taken place. Finally the tumor would show a folliculoid pattern, which corresponds to the structure presented by the gonads already differentiated. As an index of maximum differentiation, the cells would show an epithelial pattern, giving rise to the luteinized granulosa cell tumors sometimes coexisting with a differentiated structure proper of the thecomas.

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## MASCULINIZING INFLUENCE OF CYSTIC OVARIES IN FEMALE GUINEA PIGS

P. BACSICH AND G. M. WYBURN

Nature, London, 157: 588-589, 1946

About 100 guinea pigs have been ovariectomized in connection with a series of experiments on the hormonal control of reproduction. A number of animals had cystic degeneration of both ovaries, and it was noticed that these particular guinea pigs were physically very similar to the male of the species. The pathognomonic feature was the altered thoracic contour, particularly in the greater anteroposterior diameter, resulting in a postural change resembling the male. In addition, there was hypertrophy of the clitoris, and their weight exceeded that of the average female. These animals were observed for some time prior to operation, and no significant abnormalities in estrus periods or vaginal smears were noted. After operation, they responded to hormone treatment in the same manner as the spayed normal females.

There was no record of abnormal sexual behavior before operation. No histological examination was made of the ovarian cysts of these guinea pigs, but the masculine appearance, together with the absence of behavioural manifestations of heat, implies an increased androgenic influence.

It is known that the sex hormones influence not only the growing but also the adult skeleton. According to Bremer, the balance between estrogens and androgens may maintain normal control of the shape of the long bones in mammals. It is therefore assumed by the authors that an alteration of this balance by an increased secretion of androgen due to the cystic condition of the ovaries can effect the changes observed in their animals.

(No satisfactory explanation suggests itself for any causal relation of cystic ovaries with masculinization effects, and clinical experience speaks against any such effect. Most cystic ovaries are characterized by the presence of many cystic atretic follicles, with little or no hormonal effect of any kind. In one variety of cystic ovary, that often seen in association with functional bleeding, the tiny follicle cysts usually show a well preserved granulosa, and are hormonally active, producing estrogen. Since only some of the authors' guinea pigs showed a masculine appearance, it appears more likely that their mild intersexuality was of the congenital or chromosomal variety so common in the human, and that the cystic ovaries represented only a coincidental finding.—Ed.)

# LUTEOMA OF THE OVARY; A CASE SHOWING DECIDUALIZATION OF THE ENDOMETRIUM AND A HIGH PREGNANEDIOL EXCRETION RATE

GRAY H. TWOMBLY

Am. J. Obst. & Gynec., 51: 832-841, 1946

The author reports the case of a patient suffering from a rare tumor of the ovary, variously named luteoma or adrenal cortical carcinoma of the ovary, or masculinovoblastoma. This tumor is associated with amenorrhea, hirsutism, hypertrophy of the clitoris and a diabetic type of glucose tolerance curve. The chief discussion centering around this tumor does not concern its clinical picture, but rather its origin and correct nomenclature. It is thought that the present report may throw some light upon the physiological nature of such tumors and strengthen the idea that they may be functionally closely related to the corpus luteum.

The patient, a rather heavy-set 15 year old female, had, at the age of 6 years, had removed a tumor of the left upper thigh. This resulted in a permanent deformity of the left leg, causing the patient to walk with a limp.

The patient's menstrual periods had begun at the age of 11 and recurred every 28 days with rather scanty flow and slight dysmenorrhea until she was 14, when they abruptly stopped. With the amenorrhea there was an increase in body weight, deepening of the voice and increase in axillary and pubic hair. There had been no mental changes.

Examination revealed a generally feminine body contour, but there was heaviness of the shoulders and a prominence of the upper thoracic spine. The face and upper chest were covered with acneform red papules. The legs were unusually hairy, the pubic escutcheon was masculine in outline and about the margins of the areolae were numerous coarse hairs. There was a slight mustache but no beard. The voice was low-pitched and rather hoarse.

The clitoris was noticeably enlarged, and on vaginal and rectal examination a solid ovarian tumor could be felt. Since the tumor was thought to be an arrhenoblastoma, the patient was admitted to the hospital for intensive preoperative study. At the end of 2 weeks the patient complained of abdominal pain, nausea and vomiting, and the temperature and pulse rose. The tumor had rapidly increased in size to nearly 3 times its size when first examined.

Operation was performed on the following day and a freely movable, well-encapsulated smooth tumor of the left ovary, measuring 15 cm. in diameter, was removed with the left tube. The uterus and right ovary appeared normal. The patient recovered uneventfully and was discharged on the 13th postoperative day. Prior to laparotomy, a curettage was performed to obtain a specimen of endometrium.

Grossly, the tumor's main mass of tissue was grayish and somewhat gelatinous in consistency, interspersed with areas of hemorrhage. Here and there were irregular masses of yellow tissue, somewhat suggestive in outline of the wavy

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not a very satisfactory one, although perhaps convenient for those tumors of this general group in which the real origin and nature is obscure.—Ed.)

## DYSGERMINOMA OF THE OVARY

EUGENE B. POTTER

Am. J. Path., 22: 551-563, 1946

Barzilai has defined dysgerminoma of the ovary as "a germinal tissue tumor made up of cellular elements indistinguishable from the sexually undifferentiated mesenchymal cells of the early gonad."

Grossly, dysgerminomata vary widely in size from small nodules to enormous tumors. The smaller ones may retain the shape of the ovary; the larger ones become spherical or ovoid. The tumor is usually encapsulated and frequently has a knobby surface which grossly resembles brain. The cut surface is yellow to gray, rather solid and homogenous, with areas of degeneration and hemorrhage in the larger tumors.

Microscopically, the cells are large and uniform in size, the cytoplasm is granular, the nucleus is large, round and centrally placed. Basophilic nucleoli are frequently seen. The pattern which the tumor cells assume varies from a cord-like arrangement to a medullary or alveolar form. Lymphocytes are frequently found in the connective tissue, and occasionally actual lymph follicles are observed. Giant cells, resembling the Langhans' cells of tuberculosis, are often found. These cells are often seen in clumps of lymphocytes, together with epithelioid cells simulating tubercles.

A positive Friedman or Aschheim-Zondek test often is found in patients with dysgerminoma.

The author reports 4 instances of dysgerminoma of the ovary, arising in 3 females, aged 14, 11 and 18 years. The bilateral tumors in one case were not simultaneous. The left ovary appeared entirely normal at the time of the removal of an enormous tumor arising in the right ovary. Nearly 4 years later the second tumor was removed.

A Friedman test was done in 3 cases with a positive result in one and a negative result in 2.

In one case the tumor was accompanied by considerable ascites which was of recent origin since the abdomen had been struck 2 days prior to hospital admission and had rapidly enlarged following the accident. The presence of ascites has been commented on in previous reports. 8 figures.

(While the histological pattern of dysgerminoma is generally very distinctive, there are not infrequently departures from it. For example, the peripheral infiltrating portions of such a tumor often show a disposition of the cells in columns or strands instead of the characteristic picture of rather large alveoli, separated by hyalinized fibrous septa with the characteristic lymphocytic infiltration. Other variations are brought about by the extensive degenerative changes to which this group of tumors is so prone. The ages of the

pattern of the normal corpus luteum. Numerous vessels showed adherent thrombi, and it was thought that the rapid enlargement of the tumor noted clinically was probably the result of thrombosis and subsequent edema.

Microscopic examination of the tumor showed that the grayish areas were composed of polygonal or elongated cells embedded in a loose edematous collagenous stroma. The cells had rather large nuclei, each of which contained a large nucleolus. In some areas the tissue was quite cellular and the stroma dense. In others the stroma was very thin while the cells resembled embryonic fibroblasts. In the yellowish areas of the tumor the cells were distorted by huge vacuoles in the cytoplasm. The nuclei of these cells were more vesicular than in the grayish areas and there was less collagenous stroma. The vacuoles were found to be filled by globules of fat. The entire tumor was rather vascular with interstitial hemorrhage. There were no mitotic figures.

The specimen of endometrium showed almost complete decidualization.

Beginning on the 38th postoperative day the patient has menstruated regularly about every 30 days for  $2\frac{1}{2}$  years. The acne slowly disappeared. There has been a slight decrease in hairiness, but no change in the size of the clitoris or her voice has been noted. The only noteworthy postoperative change among the laboratory findings was in the glucose tolerance curve which had been diabetic in type prior to operation and now was normal.

The daily preoperative output of urinary 17-ketosteroids was about 21 mg. androsterone equivalent, or about double the normal excretion rate. Postoperatively it averaged 9.3 mg. androsterone equivalent. Urine assays for estrogen showed that the patient's amenorrhea was not due to an ovarian failure to excrete estrogens. On the day before operation 18.5 mg. of pregnanediol were found in a 24-hour sample of urine; this is considerably more than occurs in normal urines at any time during the normal cycle. Three weeks after operation there was not enough pregnanediol present in a 24-hour sample to permit assay. The inference is clear that the tumor had been acting as a functional corpus luteum producing progesterone, excreted in the urine as sodium pregnanediol glucuronide, rather than like adrenal cortex.

The author believes that this tumor is best classified under the term "luteoma." 6 figures.

(The author appears to believe that there is no distinction between luteoma and adrenal tumors of the ovary, a view which I do not think is correct, granting that in some cases the distinction may be very difficult or even impossible to make. Certainly at least one group of luteomas arises from complete luteinization of granulosa cell tumors, since all stages of this luteinization transformation may be observed in individual cases of this tumor group. In luteomas of this type the biological effect is one of feminization, due to the production of either estrogen of progesterone, or both. It is true that there are a number of case reports of luteomas which have produced masculinization, but many believe that these are really adrenal in character. The definitely adrenal tumors are always associated with masculinization. Even with the differential stains which have been suggested for the purpose, it is not always easy to establish the adrenal nature of the constituent cells. The whole question is still quite confused, and there are probably certain functional and histological interrelationships between the ovary and the adrenal cortex of which we are still quite ignorant. The designation masculinovoblastoma, suggested by Rottino, is

not a very satisfactory one, although perhaps convenient for those tumors of this general group in which the real origin and nature is obscure.—Ed.)

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author's 4 patients illustrate the tendency of dysgerminoma to occur in children and young adults ("carcinoma puellarum"). It is rare beyond middle life.—Ed.)

## STRUMA OVARIII

E. L. HELLER AND L. SPOEHR

Arch. Path., 41: 445-449, 1946

In this paper, 2 cases of struma ovarii are presented, in one of which the tumor was composed entirely of thyroid tissue. Although there was microscopic evidence of epithelial hyperplasia in one case and a large mass of ectopic thyroid tissue in both cases, the patients gave no clinical evidence of hyperthyroidism, and the authors assume that the tissue was not physiologically overactive. Cases in which struma ovarii was associated with hyperthyroidism have been observed and there have been reports of cancerous ovarian thyroid.

Thyroid tissue present in the ovary is generally regarded as a manifestation of teratomatous growth arising from totipotential germinal cells. This concept is supported by the fact that other tissue elements occur in the ovary in the majority of cases. Pure struma, composed only of thyroid tissue, does occur, though rarely. The explanation of the selective overgrowth of thyroid tissue in a teratomatous ovarian neoplasm remains obscure.

Following completion of this paper, additional sections were made from blocks of tissue from the tumor thought to be composed entirely of thyroid tissue. At one area there was a small acinus lined with columnar mucus-secreting epithelium, distinctly not thyroid in type. Although this nullifies the "pure" aspect of the struma, it supports the concept that struma ovarii is originally teratomatous. 2 figures.

(While thyroid tumors of the ovary may at times show only thyroid tissue, it is more common to find a greater or lesser degree of admixture of other teratomatous elements. As a matter of fact, it is this fact which constitutes the strongest evidence that struma ovarii is an ovarian teratoma in which the thyroid tissue to a greater or less extent, and sometimes completely, blots out other teratomatous elements. As the authors state, it is not always easy to correlate the histological appearance of the thyroid tissue of these ovaries with the occurrence or non-occurrence of hyperthyroidism. The most recent review of cases of hyperthyroidism in relation to struma ovarii is that of Emge, published in *Am. J. Obst. & Gynec.*, 40: 738, 1940.—Ed.)

## OVARIAN CYST IN THE CONTENT OF INGUINAL HERNIAL SAC

WILLIAM J. FUSARO

New York State J. Med., 46: 1024-1025, 1946

The author presents a brief summary of the literature regarding the incidence and etiology of ovarian hernia. Ovarian hernia and tubo-ovarian ectopia are

most common in children under 2 years of age. It is generally agreed that they are congenital anomalies. Ovarian hernia is also found in older age groups when the condition is aggravated by pregnancy, adhesions, etc. In children, ovarian hernia should be suspected when examination reveals a small, hard rounded mass, reducible and nontender, in the inguinal canal or labium majus. After puberty, ovarian hernia should be suspected when the patient complains of a mass in the groin which increases in size and discomfort at the menstrual periods. At pelvic examination the uterus is displaced toward the affected side and movement of the uterus causes movement of the ovary in the inguinal canal. The treatment of choice for ovarian hernia is early surgical intervention, using a Bassini type of repair, with replacement of the ovary wherever possible, depending on the absence or presence of pathology.

A case of ovarian cyst in an inguinal hernial sac, with part of the cyst intra-abdominal, and an ovarian cyst also on the opposite side, is presented. Caution never to operate for inguinal hernia in females without pelvic examination is stressed.

(In cases of pseudo-hermaphroditism especially is it important to suspect that a hernia or a firm ovoid mass in the groin is really a gonad, either an undescended testis or a herniated ovary, as the case may be.—Ed.)

## HETEROLOGOUS TRANSPLANTATION OF HUMAN MALIGNANT OVARIAN TUMOR; REPORT OF SUCCESSFUL GROWTH OF HUMAN PAPILLARY CYSTADENOCARCINOMA IN ANTERIOR CHAMBER OF EYE OF GUINEA PIG

E. G. JONES, C. W. HALE AND BERNADETTE DAMBACH

*Am. J. Obst. & Gynec.*, 51: 893-896, 1946

A tumor of the adenocarcinoma type has been grown in the eye of a guinea pig as a result of transplanting a human papillary cystadenocarcinoma of the ovary into the anterior chamber of the eye in the experimental animal. This demonstrates clearly that malignant tumors of the human ovary can be transplanted into other species where they will survive and grow. The authors suggest that this method may prove valuable in studying the morphology and physiology of ovarian tumors, and in determining their etiology.

The methods used by the authors were those which Greene has found successful in tumor transplantation, and readers are referred to his articles for details of technique. Pieces of tumor tissue over 2 mm. in diameter were introduced into the anterior chamber of the eye of guinea pigs through an opening made in the cornea. This was accomplished with the least possible trauma to the tumor and eye.

A piece of ovary, 2.5 by 2 by 1 cm., was removed at operation from a woman with an ovarian tumor so extensive that removal was impossible. The specimen

was studied histologically and the diagnosis was papillary cystadenocarcinoma of the ovary, serous type.

Transplantation was made into the anterior chamber of the eye of guinea pigs, and within 5 weeks after transplantation vascularization of the tumor in the anterior chamber was first noted in one animal. Within  $6\frac{1}{2}$  weeks this tumor had attained a size of 4 by 6 mm. Histologic examination showed that the tumor had a slightly adenomatous appearance but was generally solid, and the cells were rather undifferentiated. There were 2 spaces containing a few free cells and these were possibly the beginning of cysts. There were no papillary projections, and there was little connective tissue stroma. Hyperchromatic nuclei and mitoses were less than in the primary tumor. The tumor was surrounded by a thin capsule and the vascular supply was easily visible. The diagnosis was adenocarcinoma. 3 figures.

(This is an interesting study and the method employed may, as the authors state, prove to be a valuable means of studying the characteristics of transplanted tumors. It is evidently based on a technic similar to that of Markee in studying endometrium similarly transplanted to the anterior chamber of the eye, illustrating again how advances made in one field of research so often find rich application in others.

How far the findings reported by the authors can be applied to human problems it is difficult to say. Certainly they appear to be contrary to past views as to the inoculability or even the auto-inoculability of cancer tissue in the human. I remember hearing or reading, as a neophyte in medicine many years ago, of a dramatic experiment said to have been made upon himself by the late Dr. Nicholas Senn of Chicago, one of America's great surgeons. After operating on a patient for a very malignant cancer of the lip, he grafted a portion of the growth into his own forearm. The graft failed to take, and Senn lived for many years thereafter, dying of a different disease. Nor do I think that a surgeon would worry much about cancer if he pricked his finger during a cancer operation. And yet the experiments of the authors show that a human ovarian cancer can be transplanted to the anterior eye chamber of the guinea pig, and we have long known that certain malignant tumors of lower animals are readily transplantable.—Ed.)

## MALIGNANT GRANULOSA CELL TUMOR WITH PSEUDOTUBERCLES

H. J. SCHATTENBERG AND W. H. HARRIS, JR.

Am. J. Path., 22: 539-549, 1946

The authors present a case of granulosa cell tumor which satisfies some of the criteria for malignancy in neoplasms of this tumor group. It also presents the interesting and previously unemphasized histological finding of pseudotubercles within its structure.

At laparotomy on a 38 year old colored female, large tumors of both ovaries were encountered. There was also a yellowish brown firm nodule, 0.5 cm. in diameter, in the omentum. Bilateral salpingo-oophorectomy, hysterectomy and excision of the omental mass were performed.

On histopathological examination, the ovarian tumors were found to be made up largely of diffusely arranged cells with round dark nuclei surrounded by very

small amounts of cytoplasm. In some areas these cells were closely packed, in others widely separated. Here and there, rather well defined follicular structures with ovum-like bodies in their centers (Call-Exner bodies) were observed. Much degeneration and necrosis were present. Scattered throughout the sections were numerous pseudotubercles composed of epithelioid cells and some giant cells. The giant cells contained many nuclei arranged at the periphery in some and centrally in others. Lymphoid cells were not seen. The tumor cells showed moderate numbers of mitotic figures. In one area, lutein cells were arranged in a cyst wall; the cyst contained pink-staining homogeneous material.

Sections of the fallopian tubes showed extensive invasion with tumor cells, and invasion of the uterine musculature and endometrium was also noted. Where the endometrium was not invaded it was thickened and contained straight tubular glands compatible with the persistent proliferative phase. Some of these glands appeared dilated, but no well defined cystic structures suggestive of a "Swiss-cheese" pattern were seen. The omentum also showed collections of tumor cells similar to those in the ovaries, including the presence of Call-Exner bodies.

The pathological diagnosis was bilateral granulosa cell carcinoma of the ovaries with seeding of peritoneum and invasion of tubes and uterus, and metastatic granulosa cell carcinoma of the omentum.

The diagnosis of granulosa cell tumor in this case is based on the finding of numerous typical Call-Exner bodies among otherwise fairly typical granulosa cells arranged in a diffuse pattern. Opinion that the tumor is malignant rests on its seeding of fallopian tubes and uterus, the invasion of the uterine musculature, the fact that it is bilateral and the presence of numerous mitotic figures.

The authors believe that the best explanation for the presence of pseudotubercles is that they represent a stromal reaction to lipids derived from disintegrating tumor cells. Since this change may occur in dysgerminomas, it is plausible that a similar finding should be encountered in granulosa cell tumors which also contain lipids. 5 figures.

(Pseudotubercles of the type described by the authors are certainly not a common finding in granulosa cell carcinoma, although they are seen from time to time in dysgerminoma. The explanation suggested by the authors for the occurrence of the pseudotubercles may possibly be correct, though it would seem more likely that the pseudotubercles are an evidence of symplasmic degenerative changes, a number of cells merging their cytoplasm, while the nuclei still remain distinct.—Ed.)

## EPIDERMOID CARCINOMA ARISING IN AN ENDOMETRIAL CYST OF THE OVARY

K. McCULLOUGH, E. R. FROATS AND H. C. FALK

Arch. Path., 41: 335-337, 1946

The usual source of primary epidermoid carcinoma of the ovary is the stratified epithelial lining of a cystic teratoma. In the present case it seems to have had

another origin, the epithelial lining of an endometrial cyst of the Sampson type. It is almost impossible to diagnose such a carcinomatous transformation of an ordinary ovarian cyst and in the present case the carcinoma was only an incidental finding in material routinely examined.

The patient, an unmarried white woman, 61 years old, was admitted to the hospital with the complaint that her abdomen had been slowly increasing in size for the past 5 years, with increasing constipation for one and one-half years and lately pain in the abdomen. Her father had died of cancer at the age of 65.

Six years previously she had a growth on her lip which was treated by roentgen ray, with no recurrence or visible metastasis. For 6 days she had noted pain in the right upper abdominal quadrant. Her general appearance indicated good nourishment. Physical examination revealed no apparent abnormalities except for a slight impairment of respiratory excursion.

Operation revealed a large cyst of the right ovary, unilocular, containing an estimated 4000 cc. of thick, clear, dark brown fluid. The pedicle was attached to the right infundibulopelvic ligament and a band of tissue adhered to the posterior peritoneal wall. The cyst and the attached right fallopian tube were removed.

Histological examination of the cyst showed occasional areas which resembled endometrium and beneath this epithelium, small areas resembling endometrial stroma occurred. The thickened areas of the lining showed stratified squamous epithelium in apparent neoplasia. There were loss of polarity of the squamous cells, variation in size and shape, keratotic whorls, variation in size and pigmentation of nuclei and many mitotic figures.

In this instance the carcinoma was analogous to the epidermoid carcinoma of the uterine fundus but showed no mixture of adenomatous elements as in adenocarcinoma. It showed no evidence of teratomatous origin, no sebaceous glands, cartilage, nerve tissue or other teratoid element. The carcinoma appeared to be confined to the cyst wall, though locally invasive. No evidence of metastasis was apparent.

The postoperative course was uneventful until 3 months later when constipation and abdominal pain returned, followed by urinary frequency and pus and blood in the urine. Examination revealed a mass the size of a lemon in the left broad ligament. The patient died in another institution, following signs of uremia, and an autopsy was not obtained. 4 figures.

(Adenocarcinoma can undoubtedly arise in the wall of an endometrial ovarian cyst, as Sampson and others have shown. And so can adenoacanthoma, as could be clearly established in a recent case of my own, shortly to be reported. On the other hand, I know of no case in which epidermoid carcinoma has developed in an endometrial cyst, and such an occurrence would be even more difficult to establish than would an origin in the endometrium of the uterus itself. It is true that primary epidermoid carcinoma has apparently occurred in a very small group of reported cases, being usually explained on the basis of a previous squamous metaplasia, but the number of these is below a dozen, and some of these are questionable.)

The illustrations accompanying the authors' paper seem to justify their diagnosis of epidermoid carcinoma coexisting with endometrial cyst, but do not seem to establish that the latter is the source of the carcinoma. As the authors state, the usual origin of epider-

moid carcinoma in the ovary is from dermoid cysts. If the presence of a small dermoid lesion has been excluded by numerous sections, there remains the possibility of metastasis from the previous lesion of the lip. Unlikely though this may seem, it appears perhaps less so than an origin from ovarian endometrium.—Ed.)

## PRIMARY CARCINOMA OF THE FALLOPIAN TUBES

D. B. JUDD

Proc. Staff Meet., Mayo Clin., 21: 183-184, 1946

The presentation by the author of the following 2 cases brings the total to 18 cases of primary carcinoma of the fallopian tube seen at the Mayo Clinic from 1910 to June, 1945.

Case 1. A single white woman, 47 years of age, gave an essentially normal past history. Her menstrual periods had been regular until January, 1944, when she noticed a persistent yellowish vaginal discharge. Six months later she noticed a bloody tinge to the discharge. On examination at the Clinic on September 15, 1944, the patient stated that she had had some lower abdominal pain for a week. Physical examination was essentially negative except for a questionable cystic mass in the left adnexal region. Curettage revealed normal endometrium in the late proliferative stage. Because of the profuse, foul discharge an abdominal exploration was performed. A cystic mass was found in the left fallopian tube, and total hysterectomy and bilateral salpingo-oophorectomy were performed. The pathologic report was adenocarcinoma, grade 2, arising in the left fallopian tube. At the present report, the patient is well, except for hot flushes.

Case 2. A 50 year old white woman, who had had 2 pregnancies ending in abortion, developed metrorrhagia in 1943. A menopausal dose of roentgen rays was given in December, 1943, following which the patient progressed well until September, 1944, when vaginal discharge began. After a few months this discharge contained bloody streaks. She had no pain at any time. Examination on February 20, 1945, revealed a rather large uterus containing multiple fibromyomas and a large cystic mass in the left adnexal region.

At laparotomy, a large cystic tumor was found filling the left side of the pelvis and adherent to the abdominal wall. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The pathologic report was adenocarcinoma, grade 2, arising in a fallopian tube. Because the tumor was adherent and was ruptured in removal, the patient received a course of high voltage roentgen treatment before dismissal. Nearly 6 months later she was well and pelvic examination was negative.

(While I happen to be one of those who do not believe that the vaginal smear method is likely to displace biopsy and curettage in the decisive diagnosis of cervical and corporeal cancer, it would seem to me to have definite application in cases in which primary tubal

carcinoma is suspected. Such lesions are of course beyond the reach of biopsy, but there should be no difficulty in finding desquamated carcinoma cells in the vaginal smear, provided that one is adequately trained in this technique. However, this disease is very rare, so that its presence is likely to be not even suspected before operation.—Ed.)

## GENITAL TUBERCULOSIS IN WOMEN

ARCHIBALD L. McDONALD

Am. J. Surg., 71: 748-751, 1946

The clinical picture of genital tuberculosis is not sufficiently characteristic nor sufficiently recognized to permit accurate clinical diagnosis, even by experienced clinicians. Greenburg, in a review of 200 proved cases, gives the frequency as follows: one per cent of all gynecological cases, 8 per cent of all pathological Fallopian tubes, and one in 13 cases diagnosed clinically as chronic pelvic inflammatory disease. A correct preoperative diagnosis was made in only 13 per cent of the series, and  $\frac{1}{2}$  of these had ascites and obvious tuberculous peritonitis.

The author emphasizes that tuberculosis as a cause or complication of pelvic disease must be given serious consideration in the clinical study of women patients in order to avoid surgery at an unfavorable time or in the presence of unrecognized pulmonary disease, and so that the surgeon may recognize the nature of the lesion and carry out adequate measures, namely, the removal of all diseased tissue.

Tuberculosis of the female genital organs is but a part or complication of constitutional disease with the primary focus in the lungs. While theoretically possible, primary involvement of the cervix or lower genital tract is rare. The infection is carried in the blood to the mucosa of the Fallopian tubes which is the primary pelvic or peritoneal lesion. The primary lesion in the tubal mucosa undergoes the characteristic tuberculous processes, and extension takes place into the fundus of the uterus and to the opposite tube, the condition found in most laboratory specimens. Tuberculous peritonitis is usually due to lesions in the Fallopian tubes and can be cured by removal of the pelvic focus of infection.

In regard to removal, the following facts should be borne in mind: (1) The tuberculous lesion may be adherent to the bowel or bladder and careless handling may cause a fistula. (2) Drainage is to be avoided since secondary infection may result in a persistent sinus. (3) Incomplete excision of the lesion will leave a focus for spread of the disease and exacerbation of the process. The cervix is involved late in the process, likewise the ovaries. Therefore, adequate excision should include subtotal hysterectomy with both tubes unless the cervix is known to be involved. If the ovaries are grossly normal, they may be left at the discretion of the surgeon. After surgery, these patients should be kept under careful observation to detect any possible recurrence of the pulmonary disease.

(Although Greenburg's figure of an incidence of 8 per cent of tuberculosis among pathological tubes was based upon a study made in our own laboratory, I would be inclined to think it a little high, and that something like 5 per cent would be more nearly correct. The small percentage of cases in which a correct preoperative diagnosis was made is of interest, but is in conformity with general experience. As a matter of fact, the diagnosis is not usually made even at operation, except in the minority of cases presenting tubercles on the serous surface. This is uncommon except with advanced cases and those associated with tuberculous peritonitis. The so-called tobacco-pouch appearance of the fimbriated end often gives an inkling as to the tuberculous nature of the disease, but it may be absent or misleading.)

There are still differences of opinion and practice as to the extent of operation in these cases. In spite of the reparative tendency of the tuberculosis in some of these cases, subsequent pregnancy is rare, so that removal of the tubes is indicated. In the milder forms some surgeons conserve the uterus, trusting to the healing powers of nature to throw off the uterine involvement, which is present in a large proportion. On the other hand, since later pregnancy is highly improbable anyhow, it seems to me safer to remove the uterus also.—Ed.)

## MESONEPHROMA OF THE FALLOPIAN TUBE

H. F. CONNALLY, JR.

Am. J. Obst. & Gynec., 51: 904-907, 1946

The case is presented of a 32 year old woman who reported to the outpatient department complaining of lower abdominal pain. Premenstrual tension, dysmenorrhea and hypomenorrhea were also evident. Pelvic examination revealed a cyst the size of an orange rising from the right adnexal region. The uterus was enlarged, and a myoma was noted in the anterior wall.

At operation a smooth cyst was found replacing the right ovary. The uterus contained intramural myomas. The left ovary appeared to be normal but in the lateral third of the left tube a firm, solid fusiform tumor, 1 cm. in diameter and 2 cm. in length, was noted. Oophoro-cystectomy, right, bilateral salpingectomy and subtotal hysterectomy were performed.

The unilocular thin-walled ovarian cyst proved to be a simple serous cystadenoma showing no papillary tendencies. The uterus contained intramural and subserous myomas. Chronic salpingitis was observed microscopically in the right Fallopian tube.

The tumor of the left tube was located within the wall of the tube and the serosa was smooth and freely movable over the tumor. Grossly the tumor was yellowish-white in color and was solid. Microscopically the tumor showed a tubular-like pattern. In some portions tiny cystic areas were noted, lined by a single layer of flattened cuboidal epithelial cells containing vesicular nuclei of moderate size. Hydropic tendencies were noted more frequently toward the periphery of the tumor, and occasionally bulging nuclei were demonstrated. Variation in degree of differentiation was clearly noted throughout the sections.

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## FEMALE UROLOGY

### THE VAGINAL INTERPOSITION OPERATION AND ITS MODIFICATIONS FOR UROLOGICAL CONDITIONS

ALBERT PHILIP

Urol. & Cutan. Rev., 50: 206-208, 1946

The author believes that interposition is a good basic operation especially suited to patients who are at or near the menopause and who have large cystocele complicated by urethrocele, urological complaints and stress incontinence. A brief description of interposition is presented. After preoperative preparation, disinfection and exposure, the cervix is pulled down. The anterior vaginal wall is dissected, starting in the midline and proceeding laterally, making wide vaginal flaps on both sides. These flaps should be thin, leaving all muscular and fascial tissues in place on the bladder. The dissection proceeds laterally under the pubic bones and to about  $\frac{1}{2}$  inch below the urethral opening in the midline. A careful dissection of the bladder from the cervix follows. Traction on the bladder will facilitate location of the cleavage area. Then, pushing up the bladder, the anterior pouch is reached and opened widely enough to bring forward the uterine body. The so-called pillars of the bladder are left intact. The adnexae are investigated. At approximately the region of the internal os, the bladder peritoneum is sewed to the posterior wall of the uterus. If the uterus is of proper size it can then be transposed between the bladder and vaginal wall; its position should be just below the symphysis. The region of the round ligament insertion is transfixed with a strong suture and sewed to the pubic ligaments and surrounding tissues on both sides. Abundant vaginal flaps are dissected and the vaginal wound closed, including uterine tissues in the sutures. The operative procedure is completed by the performance of colpoperineorrhaphy.

The author discusses modifications of the basic procedure which are required in certain conditions. Vesico-vaginal transposition of the uterus and its modifications is to be highly recommended for certain selected cases. The surgeon who is experienced in vaginal work can modify his original plan as he operates, according to the need and circumstances.

(Any of the common cystocele repair procedures lend themselves very readily to correction of the stress incontinence so often seen with cystocele, especially when it is combined with urethrocele. The complete interposition operation, as described by the author, is not nearly as popular as formerly. In most cases some type of the so-called advancement operation, combined with the Manchester procedure of suturing the cardinal ligaments anterior to the cervix, is just as effective and often much simpler. It can be readily combined with some such procedure as that of Kennedy for the correction of incontinence. When the bladder neck is very baggy and prolapsed, a vesical plication of the Kelly type is of additional value.—Ed.)

Cell height was increased, and in some areas the lining epithelium appeared to be multiple in place of the typical single layer. The author failed to note any structures resembling glomeruli. Mitotic figures were conspicuously absent.

Sections were reviewed at the Army Medical Museum and by Dr. Emil Novak and Dr. G. E. Seegar Jones. In each instance the suggested diagnosis was mesonephroma.

The author believes that this tumor may represent a very early phase of Schiller's case Number 1. 4 figures.

(This tumor, sections of which Dr. Connally kindly permitted me to see, is a very unusual one, and I could think of no other probable origin than mesonephric structures, in view of its location and histological structure. I have seen one other tumor which resembles it, though not exactly, and this appeared to rise from the broad ligament adjoining the ovary, but not involving the latter. This patient has remained well since her operation about 12 years ago. The designation mesonephroma would seem perhaps more justifiable for this tumor type than for the "mesonephroma" described by Schiller. While the pattern of the latter is quite distinctive, there is still much doubt as to its mesonephric origin.—Ed.)

A woman of 64 was admitted to the hospital on January 20, 1944. Since November, 1943 she had had dysuria and frequency, the nocturia amounting to 4 times. Early in January she had noticed hematuria which subsided with bed rest. On January 15 she experienced loss of bladder control and felt "something coming out of the vagina" on straining for urination and defecation, which receded spontaneously during sleep or on being pushed back.

At the time of hospital admission, the patient's temperature was 100, pulse regular, respiration 18, and blood pressure 140/90. Physical examination was essentially negative. Urinalysis of a catheterized specimen showed: specific gravity, 1.010; reaction, acid; albumin, 2 plus; sugar 0; microscopic examination, innumerable clumped leucocytes, 10 to 12 red blood cells per high power field; epithelial cells, 1 plus. A culture yielded *B. coli*.

At cystoscopy, the urethra and internal vesical sphincter were wide and their mucosa folded on itself longitudinally. The bladder vessels were injected, but the mucosa between them was pale. On the trigone the mucosa was edematous and heaped in folds. The right half of the trigone and region of the right ureteral orifice were obscured by a large tumor, estimated at thumb to walnut size, covered by reddened puckered mucosa with fibrin adherent to its tip. Its base took origin just inside the internal bladder sphincter, and seemed quite broad, occupying  $\frac{1}{2}$  the trigone.

At the time of prolapsus the vulva revealed a little leakage of urine. A tumor approximately 2 by 3 cm. occupied the urethral orifice and obscured the vaginal introitus. The tumor was soft throughout with fine minute strands of fibrin adherent to its tip. A dimple on its top side suggested an orifice and easily admitted a No. 6 F. catheter to 35 cm. without obstruction. The diagnosis was intermittent prolapsus through the urethra of a large right ureterocele; subsiding acute right pyelitis and cystitis; slight impairment of right kidney function mild ureterectasis; and pelvic stasis.

Normal saline was injected to try to expand the cyst, but a second opening below was discovered. An elliptical piece of tissue, including both openings, was removed and the remaining cyst was lightly electrocoagulated. Ten days after operation a catheterized specimen of urine contained no albumin, and on microscopic examination only epithelial cells and amorphous urates. The patient had been entirely free of symptoms when seen in November, 1945. 5 figures.

## THE "INTRACTABLE" VESICO-VAGINAL FISTULA

CHASSAR MOIR

Brit. M. J., 1: 774, 1946

The author refers to a recent publication by Mackay reporting spontaneous closure of a large vesico-vaginal fistula, stating that it is useful to remember that this injury, so often regarded as intractable, is possessed of a strong tendency to spontaneous cure. This is particularly true when the fistula is the result of tearing of otherwise normal healthy tissue rather than the loss of tissue by necrosis.

In most cases, difficulty of exposure of the fistula at operation may be overcome by the use of a generous episiotomy and the adoption of the knee-chest position. The author has found Grey Turner's modification of this position most helpful. The anesthetized patient is placed, face down, low on the table with the legs flexed at the hips and the knees placed on, and bandaged to, a low stool. The table is then lowered so that the pubic region is just clear of the top.

The author does not support a pessimistic attitude toward the curability of vesico-vaginal fistulas. In his experience with 30 cases, it has been possible in all of them to repair the fistula by the vaginal approach alone, using, for the most part, a simple Sims' type of operation.

The most difficult case is that in which there has been extensive tissue loss at the vesico-urethral junction. Subsequent severe stress incontinence of urine may sometimes be relieved by the use of a pessary to press on the urethra, or, more certainly, by the use of the Aldridge fascial-sling operation.

(Every gynecologist of experience has noted the occasional spontaneous closure of either vesico-vaginal or, even more often, of uretero-vaginal fistulas, though such a happy outcome is not often to be expected in those of any size. The healing of small vesico-vaginal fistulas is greatly favored by the employment of a retention catheter and postural treatment, the patient being kept in the prone position. It is of interest to note that Moir, who is professor of obstetrics and gynecology at the Oxford University Medical School, is so partial to the Sims type of operation. Certainly this is still a highly satisfactory procedure in a considerable proportion of cases. In the larger fistulas with indurated cicatricial margins and much fixation, I believe that the flap-splitting procedures, with free mobilization of the bladder wall, are more likely to give successful results.—Ed.)

PROLAPSUS OF A URETEROCELE THROUGH THE URETHRA:  
CASE REPORT

MARIE ORTMAYER, LOUISE KOESTER AND PERLE M. STETLER

J. Urol., 55: 515-519, 1946

Thirty-eight cases of prolapsus of a ureterocele through the female urethra were found in the available literature, attesting the rarity of this condition. The authors present an additional case report.

A woman of 64 was admitted to the hospital on January 20, 1944. Since November, 1943 she had had dysuria and frequency, the nocturia amounting to 4 times. Early in January she had noticed hematuria which subsided with bed rest. On January 15 she experienced loss of bladder control and felt "something coming out of the vagina" on straining for urination and defecation, which receded spontaneously during sleep or on being pushed back.

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Thirty-eight cases of prolapsus of a ureterocele through the female urethra were found in the available literature, attesting the rarity of this condition. The authors present an additional case report.

(31.7 per cent). However, many clinically suspected fibroids were later found to be nonexistent or very small. The significant finding in the cataloging of palpable diseases is the fact that 18.6 per cent of all the women operated upon were recorded as having no disease of the pelvic organs. This absence of palpable disease may, in part, be explained on the basis that the patient may have had troublesome symptoms, without gross disease of the pelvic organs, but even so, this figure seems high.

It is startling to note that, among the pathologists' findings, 30.8 per cent of the organs removed showed no histopathology. The facts that 17.4 per cent presented no symptoms, and 18.6 per cent had no palpable pelvic disease, do not permit the conclusion that nearly one-fifth of these patients had *remunerative* hysterectomies. Asymptomatic neoplasms may have required removal and patients revealing no palpable disease may have suffered from blood loss due to a hidden disease. However, the fact that 76, or 30.8 per cent, of the 246 patients operated upon were found to be free of pathology, is a stunning observation which cannot easily be accounted for.

Correlation of cases presenting no histopathology, no symptoms and/or normal pelvic findings shows that 17.1 per cent of patients had neither symptoms nor pathology, 18.7 per cent had neither palpable nor microscopic disease, while 16.6 per cent had neither symptoms, suspected disease on pelvic examination, nor microscopic disease in the removed organs.

In 49.7 per cent of the 246 patients, the clinical diagnosis was confirmed. In 17.4 per cent, the clinical diagnosis was not confirmed, but the operation was considered justifiable. In 33.1 per cent of the cases there was either no disease or else disease contraindicating hysterectomy.

(It is probable that the results of this analytic study will not be a tremendous surprise to most readers, because everyone who has eyes to see and ears to hear must know that the operation of hysterectomy has been shamefully abused throughout this country, and probably others as well. It is not necessary to comment on Miller's figures, because they speak for themselves, and his standing makes his findings authoritative. What he says as to unnecessary hysterectomy applies equally well to unnecessary removal of "cystic ovaries", just as, in the field of general surgery, it applies to unnecessary appendectomies for wrongly diagnosed chronic appendicitis.

The great bulk of gynecological operations are of the elective type, but there should be a clear indication even for these. If the patient recovers from the operation she, and perhaps the surgeon too, are apt to speak of the operation as "successful." In this sense a man might be very successfully castrated, but would he be happy about the operation if he knew there was no need for it? Just as there are honest business men and those who are sharp and unscrupulous, so there will probably always be honest and conscientious surgeons, as opposed to a minority who are slipshod and not overburdened with conscience. A pretty safe rule, which would impose severe handicap on at least some surgeons, would be to ask themselves if, under the given conditions of any case, they would recommend the contemplated operation if the patient were one of their own family.—Ed.)

## OPERATIVE GYNECOLOGY

### HYSTERECTOMY: THERAPEUTIC NECESSITY OR SURGICAL RACKET?

NORMAN F. MILLER

Am. J. Obst. & Gynec., 51: 804-810, 1946

Once a rare and spectacular feat, performed only by experienced and courageous surgeons, hysterectomy has become quite commonplace, and the indications, once highly restricted, have been so broadened as to warrant scrutiny and re-evaluation. Medical progress is altering the practice of surgery; chemotherapy and hormonal therapy may make it necessary to re-evaluate the indications for pelvic surgery.

In order to learn something of the prevailing attitude regarding hysterectomy in both large and small communities, the author undertook the present study based on 246 hysterectomies. These represent hysterectomies performed during the first 4 months of 1945 in 10 different hospitals. This report attempts to correlate symptoms and physical findings with the histopathology actually observed.

The 246 hysterectomies were distributed among various age groups as follows: under 20 years, 1 case; 20-29 years, 30 cases; 30-39 years, 78 cases; 40-49 years, 108 cases; 50-59 years, 22 cases; 60-69 years, 6 cases; and 70-79 years, 1 case. There were 4 postoperative deaths, a mortality rate of 1.6 per cent. This may be compared with a low of 0.6 per cent and a high of 4.64 per cent reported in the literature.

There was evidenced a definite preference for the incomplete or subtotal excision over the total by more than 2 to one. The author prefers the total operation for the obvious reason that future disease of the cervix is eliminated, but questions other advantages claimed for complete hysterectomy. A correlation between the various age groups and type of hysterectomy was made to determine whether concern over the cervical stump as a site for carcinoma later in life was reflected in a higher incidence of total hysterectomy in the older age groups. No such concern was evidenced, since the subtotal operation still predominated during the 4th and 5th decades.

The chief symptom leading to medical care in this series of patients was bleeding (41.4 per cent). Other complaints included abdominal pain (9.7 per cent), pelvic pain (7.7 per cent), and backache (5.2 per cent). Almost 10 per cent sought medical care for secondary symptoms such as fatigue, nervousness and headache. It is interesting to note that 17.4 per cent of the patients, subjected to major surgery, had no complaints. This may be due, in part, to the finding of asymptomatic conditions on routine pelvic examination.

The predominating physical finding on digital examination was uterine fibroids

missed with the eurette, as can happen in a large myomatous uterus, the surgeon can include bilateral removal of the adnexa with the hysterectomy. Certainly the gynecologist must always bear in mind the possibility that bleeding is not necessarily due to the gross and readily demonstrable lesion which he finds, but may be due to an associated and less easily demonstrable one concealed within the uterus. But no blanket rule of procedure can be laid down for the study and management of all cases.—Ed.)

### MENSTRUAL CONSERVATIVE HYSTERECTOMY (PREVIOUS INSTILLATION OF COLORED CONTRAST WITHIN THE UTERINE CAVITY)

LICINIO H. DUTRA (Sao Paulo, Brazil)

An. Bras. de Ginec. (Rio de Janeiro, Brazil) 19: 3-7, 1945

The author reports a new technic to locate more easily the endometrium when performing the conservative type of hysterectomy, mainly when large fibromyomas are present.

It consists of an intrauterine instillation through the cervix, just previous to the operation, of a 2.5 per cent methylene blue solution (3 to 5 cc.). The endometrium, thereby, becomes easily recognizable by contrast from the adjacent tissues.

The author has been trying to find a solution that would act at the same time as a strong dye and as a bacteriostatic. For this purpose, a mixture of a 2.5 per cent solution of methylene blue with penicillin (2000 "O.U.") may prove to be the best.

Following this detail and by means of the use of the hemostatic tourniquet, the author has been able to perform with success the so-called menstruation-conservative hysterectomy, thus saving large portions of endometrium and maintaining the vascular and nervous systems of the adnexa, in obedience to the theory of functional endometrium-ovarian synergism.

(This simple procedure might perhaps be of some value, though even without it there is rarely any difficulty in recognizing the endometrium in operations of the type for which the author recommends it.—Ed.)

### THE COMBINED MANCHESTER-WATKINS INTERPOSITION OPERATION IN THE TREATMENT OF PROLAPSE OF THE UTERUS

B. Z. CASHMAN

Am. J. Obst. & Gynec., 51: 706-707, 1946

The author has found a combination of the Manchester operation and the Watkins interposition procedure to be satisfactory in the treatment of first- or second-degree prolapse when accompanied by a very large cystocele.

## "SUBTOTAL HYSTERECTOMY" FOR CANCER OF THE CERVIX AND UTERUS

West. J. Surg., 54: 211-212, 1946

Attention is drawn to the importance of curettage prior to hysterectomy to exclude the possibility of cancer of the uterine body or endocervix. If the average "fibroid uterus" required the surgical skill demanded by a partial gastric or bowel resection, and carried with it equal complications and risks, fewer uterine amputations would be done without knowing beforehand that the tumor was actually benign and the operation indicated. If the cause of symptoms is endometrial carcinoma, then either a panhysterectomy is indicated, or, with involvement of the cervical segment, radiation alone is the treatment of choice.

When there is cancer of the cervix arising in the endocervical canal, then supracervical hysterectomy is disastrous and deprives the patient of the maximum benefit to be derived from subsequent radiation therapy. In the absence of the uterine canal adequate radium therapy for uterine or cervical cancer is impossible.

The scrapings obtained at curettage should be given careful histological examination. Also, it is reemphasized that for diagnostic purposes it is important to curet the endocervical canal separately from the uterine canal, and to send the specimens to the pathologist labeled as such. In addition to the curettage a biopsy of the cervix should be made, so that it may be known whether or not an adenocarcinoma has arisen in or spread down to involve the cervical segment of the uterus. In such a case, radiation therapy alone should be used.

The additional cost to the patient of a curettage prior to hysterectomy is small, in comparison with the cost in longevity, suffering and money which will result from incomplete operation involving an unsuspected cancer.

(While there are of course some cases, more particularly those of abnormal bleeding of indeterminate source, in which the meticulous preliminary investigation advocated by the author is clearly indicated, I do not believe that this is called for in every case in which hysterectomy is contemplated. For example, it would seem to be carrying thoroughness too far, in the case of a nulliparous woman with a large myoma and with a very clean cervix and no abnormal bleeding to subject her to two operative procedures as advocated by the author. Moreover, I believe that there is somewhat more risk of infection if hysterectomy is done within a few days of curettage, which often and possibly always causes some degree of endometrial infection, not to speak of the economic and mental burden of two operations and anesthetics within a few days.

There are two other routine procedures which, to my mind, are much more important before and during hysterectomy operations. One is thorough examination of the cervix, not only by palpation but by inspection in the best possible light. Should there be any lesion in any way suspicious, biopsy should of course be done. This will avoid leaving behind a carcinomatous cervix should the operator employ the subtotal technique, and such an accident explains a considerable proportion of the many reported cases of cancer in the residual stump. Most of us now do total hysterectomy unless there is some important contraindication, but even so preliminary investigation of the cervix is important, because its results may very definitely change one's plans of management of the case.

The other simple precaution which deserves mention is that of having the uterus laid open in the operating room as soon as it is removed, whether or not preliminary curettage has been done. If by any chance a symptomless carcinoma is present, or a lesion has been

missed with the curette, as can happen in a large myomatous uterus, the surgeon can include bilateral removal of the adnexa with the hysterectomy. Certainly the gynecologist must always bear in mind the possibility that bleeding is not necessarily due to the gross and readily demonstrable lesion which he finds, but may be due to an associated and less easily demonstrable one concealed within the uterus. But no blanket rule of procedure can be laid down for the study and management of all cases.—Ed.)

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The other simple precaution which deserves mention is that of having the uterus laid open in the operating room as soon as it is removed, whether or not preliminary curettage has been done. If by any chance a symptomless carcinoma is present, or a lesion has been

sympathectomy of the inferior mesenteric artery, resection of the lower portion of the aortic plexus and lumbar sympathectomy in 3 cases.

Since abdominopelvic sympathectomy increases the blood supply and the development of the collateral circulation of the pelvic organs, the author tried to lessen the risk of hemorrhage at the level of the ulcerated cancer by bilateral ligation of the hypogastric arteries. However, it is to be noted that, even when bilateral ligation of the hypogastric arteries is performed, after the operation there is an evident increase in the development of the collateral circulation, as the author has already demonstrated in experimental investigations. In the present series of 14 cases, after the abdominopelvic sympathectomy, there was no death caused by hemorrhage.

In order to analyze the influence of the increased blood supply caused by abdominopelvic sympathectomy in the development of the cancer, in 2 cases resection of the hypogastric plexus was preceded by treatment by irradiation, and in 5 cases radium was applied postoperatively during the phase of vasodilatation of the pelvic vessels. The results obtained reveal that when abdominopelvic sympathectomy was preceded but not followed by irradiation, there was quick recurrence and development of cancer of the cervix. Much better results were obtained when the application of radium was performed during the increased blood supply caused by vasodilatation following the sympathetic operation.

The extensive abdominopelvic sympathectomy, in which resection of the lower portion of the aortic plexus was added to resection of the hypogastric plexus, lumbar sympathectomy and periarterial sympathectomy of the common iliac, hypogastric or mesenteric arteries, demonstrated that the visceral sympathetic pain remains relieved during the period in which the cancer remains within the anesthetized area. If the cancer progresses and invades the lumbosacral plexus, pain appears, radiating down to the lower extremity. As there may exist a sympathetic or a somatic pain or both in cancer of the cervix uteri, two therapeutic problems, the one sympathetic and the one somatic, must be analyzed according to the type of mechanism of pain. From these investigations it is deduced that abdominopelvic sympathectomy relieves only the visceral sympathetic pain and must be followed by adequate treatment with radium and the roentgen ray. 5 figures.

(The procedure described by the author is a far more formidable one than the comparatively simple presacral sympathectomy which some have employed for relief of the intractable pain of advanced cervical cancer. Since his results do not appear impressive, the method cannot be said to commend itself, as the author would probably agree. The problem of the hopeless cancer patient is really a very grave one, aside from the suffering of the individual patient, because it so commonly falls upon the family to see the poor victim through her terminal months of suffering. One of the crying medical needs of the country is an increase in hospital facilities for the care of these hapless sufferers, who so often, after the failure of the radiotherapy or surgery which hospitals provide, are wished back on the family and the family doctor to end their days. In my town the institutional facilities for the care of such advanced patients are almost nil, and this must be a common condition throughout the country. While such procedures as alcohol injection, sympathectomy and chordotomy have probably been helpful in the relief of pain in some cases, morphine still continues to be the best friend of most of these sufferers in their terminal days.—Ed.)

The Manchester operation is carried out in the usual way, with or without amputation of the cervix. The sutures in the stumps of the divided cardinal ligaments are placed, but not tied. The anterior cul-de-sac is then opened and the uterine fundus brought out and interposed, as in the Watkins procedure. All sutures are then tied and the operation completed by doing a high posterior colporrhaphy to narrow the vagina and to care for a high rectocele. This is followed by a perineorrhaphy.

Since 1939, 15 combined Manchester-Watkins interposition operations have been performed, with follow-up study of 10 patients. One woman, 72 years of age with cardiovascular disease, died at home of coronary thrombosis 3 weeks after leaving the hospital. One patient complained of backache, leucorrhea and dizziness. The anatomic results were good in all cases, with no recurrence of cystocele or prolapse.

(The operation described by Cashman is a good one, and I believe it represents about what would be done for similar indications by most gynecologists. The Manchester procedure of bringing the cardinal ligaments together in front of the cervix is not in itself sufficient to cure an associated cystocele or cysto-urethrocele. On the other hand, it is rarely necessary to interpose the uterus beneath the bladder, as is done in the original Watkins operation and as Cashman advises, since practically always the modified Watkins or advancement operation is just as effective. Of great importance is the closure of the suburethral space, as otherwise there is danger of recurrence of a cysto-urethrocele. For this I employ a triangular stitch embracing the fundus in the middle and the strong sub-pubic ligaments at each side. The cardinal ligaments need not always be cut before their suture anterior to the uterus, as the same result can usually be accomplished by simply sewing them snugly together in the midline. Assuming of course that the patient is beyond the child-bearing age, it is generally wise to amputate the cervix unless it is short, atrophic and grossly of entirely normal appearance. In no field of gynecological surgery is it more important to fit the operation to the patient rather than vice-versa.—Ed.)

## ABDOMINOPELVIC SYMPATHECTOMY FOR RELIEF OF PAIN OF CANCER OF THE CERVIX

A. DE SOUSA PERERIA

Arch. Surg., 52: 113-134, 1946

In order to determine the value of abdominopelvic sympathectomy in the treatment of intolerable pain in cancer of the cervix uteri, the author has performed a series of sympathetic operations on 14 patients. These operations were limited to resection of the hypogastric plexus in 7 patients, but in the remaining patients there was added one or more of several other operations. Thus, sympathectomy of the hypogastric arteries was added in one case; sympathectomy of the right common iliac artery in one case and of the common iliac and inferior mesenteric arteries in one case; sympathectomy of the inferior mesenteric artery and resection of the lower portion of the aortic plexus in one case; and finally,

sympathectomy of the inferior mesenteric artery, resection of the lower portion of the aortic plexus and lumbar sympathectomy in 3 cases.

Since abdominopelvic sympathectomy increases the blood supply and the development of the collateral circulation of the pelvic organs, the author tried to lessen the risk of hemorrhage at the level of the ulcerated cancer by bilateral ligation of the hypogastric arteries. However, it is to be noted that, even when bilateral ligation of the hypogastric arteries is performed, after the operation there is an evident increase in the development of the collateral circulation, as the author has already demonstrated in experimental investigations. In the present series of 14 cases, after the abdominopelvic sympathectomy, there was no death caused by hemorrhage.

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(The procedure described by the author is a far more formidable one than the comparatively simple presacral sympathectomy which some have employed for relief of the intractable pain of advanced cervical cancer. Since his results do not appear impressive, the method cannot be said to commend itself, as the author would probably agree. The problem of the hopeless cancer patient is really a very grave one, aside from the suffering of the individual patient, because it so commonly falls upon the family to see the poor victim through her terminal months of suffering. One of the crying medical needs of the country is an increase in hospital facilities for the care of these hapless sufferers, who so often, after the failure of the radiotherapy or surgery which hospitals provide, are wished back on the family and the family doctor to end their days. In my town the institutional facilities for the care of such advanced patients are almost nil, and this must be a common condition throughout the country. While such procedures as alcohol injection, sympathectomy and chordotomy have probably been helpful in the relief of pain in some cases, morphine still continues to be the best friend of most of these sufferers in their terminal days.—Ed.)

DIFFICULTIES AND ACCIDENTS ENCOUNTERED IN  
CONSTRUCTION OF THE VAGINA

LAWRENCE R. WHARTON

Am. J. Obst. &amp; Gynec., 51: 866-875, 1946

The author presents a resumé of the common difficulties and complications that have been encountered in construction of the vagina. In general, the simplest technique that is compatible with attaining a good result is recommended.

Care in the selection of patients as candidates for the operation will obviate some failures. The best results have been obtained in young women, recently married or about to be. If the constructed vagina is not used, it will probably contract. In women having no ovaries, a satisfactory vagina can be made and maintained if it is used often. In the absence of ovaries, one can use Thiersch grafts, and thus avoid dependence upon the proliferation of vaginal epithelium. The author's choice of operation lies between 3 procedures—the Frank procedure, the author's operation, or the operation of Graves. He has used Thiersch grafts, to hasten epithelization, for several years.

The dissection of a large space is essential. The space should be deep (11 to 13 cm.), wide, and the vaginal orifice wide enough to admit 3 fingers. In dissecting out the space, one may encounter difficulties, especially in patients who have had similar operations before. In such cases, dissection is always fraught with danger to the rectum and bladder.

With proper precautions, infection and hemorrhage rarely occur. Perforation into the bladder or rectum may occur during operation or later during the convalescence. During the dissection of the vaginal space, there is not much danger of injuring the rectum or bladder if the plane of cleavage is normal. However, in patients who have had former dissection in this region, the plane of cleavage is replaced by scar tissue and injuries to bladder and rectum are common under these circumstances. To help prevent postoperative rectal perforations, the vaginal form should be long enough so that it projects somewhat from the vagina. Also, the vaginal orifice should be large enough for the form to escape readily if the intrapelvic pressure is unduly increased.

Aftercare of these cases is simple. The form remains in the vagina for 3 weeks; it is then removed and the vagina inspected and cleaned. The process of epithelization is observed and a biopsy may be taken. The form should be worn most of the time after that for a month, depending on the process of epithelization. After that, it is worn only part of the time, at night, if necessary. Coitus is begun carefully after epithelization is firm and complete. 7 figures.

(For most cases it seems to me that the operation described by the author is the one of choice. It is simple and gives good results, even if Thiersch skin transplants are not used, though the latter no doubt accelerate epithelization. I believe that the late accidental perforation of the rectum reported by the author in one of his cases is the only one thus far recorded. To avoid this, he recommends that the vaginal obturator be long enough to

project somewhat beyond the introitus, but I would think that, aside from some annoyance to the patient, there would be greater likelihood of losing the plug. Perhaps it would be wiser not to select a too ambitiously long vaginal form, and thus avoid the risk of undue pressure on the rectum.—Ed.)

## INTESTINAL OBSTRUCTION IN GYNECOLOGY

E. J. BATEMAN

*Am. J. Obst. & Gynec.*, 51: 666-671, 1946

The gynecologist should be an abdominal surgeon able to recognize and to deal competently with intestinal obstruction. The author presents a discussion of the points in diagnosis and general principles of treatment of this condition.

In the study of any new admission, a history of failure to move the bowels for 48 hours, or even less if frequent vomiting is present, should make one conscious of the possibility of obstruction. If, in addition to frequent vomiting, even moderate distension is present, together with colicky abdominal pain, loud gurgling peristalsis and localized tenderness, the diagnosis is clear. Obstruction can result from severe pelvic inflammatory disease, from some pelvic tumors, post-operative adhesions, any tumor of the intestinal tract or strangulated hernia. Malignancy of the pelvic colon may at times be wrongly diagnosed as disease of the left adnexa.

The development of postoperative intestinal obstruction must be suspected whenever "gas pains" become too frequent and persistent, especially if the patient indicates a fairly definite point of maximum intensity of the cramp. Vomiting, loud gurgling peristalsis and tenderness complete the diagnostic picture.

In regard to treatment, if the diagnosis is made within 24 or 48 hours of the onset of symptoms and the patient's general condition is good, immediate operation should be performed. If the diagnosis is made later, after distension and water and chloride loss have become marked, operation must be deferred until these conditions have been improved as far as possible. Operation for the relief of intestinal obstruction should be done rapidly and with a minimum of trauma.

(Although this complication is fortunately not extremely common, it is one to be dreaded, and its recognition may tax the judgment of the surgeon about as much as any that I know. Many laparotomy patients have a disturbing amount of distention, pain and vomiting for a day or two after operation, and the surgeon is made happy when such measures as the nasal tube, glucose and prostigmin are followed by relief. If they continue and increase, with no passage of flatus or feces, the strong possibility of obstruction must arise in the surgeon's mind. It is distressing to have to think about re-operation in patients who have just passed through serious abdominal operations, and yet too long delay means that the golden moment will slip by. During this anxious waiting period the patient should be given the benefit of such preparatory measures as the author has mentioned. In most cases spinal anesthesia should be the choice. At operation the gynecologist does have the advantage of knowing that the obstruction is most likely to be in the pelvic operative field, usually a

band of adhesions or the fixation of an intestinal loop to some raw area. Gentle palpation will often reveal this without too much handling of the bowel, and attention can then be centered on the area of block. If operation has not been too long delayed, the liberation of the obstructed block is all that is required.—Ed.)

## A POSSIBLE HEPATIC (HEPATORENAL) FACTOR IN GYNECOLOGIC MORTALITY

MELVIN D. STEINER

*Am. J. Obst. & Gynec.*, 51: 678-684, 1946

The author discusses the possibility of the occurrence of the so-called "liver" and "liver-kidney" deaths after gynecological surgery and presents an analysis of 10 deaths occurring at the Charity Hospital of Louisiana from 1937 to 1940, in which the hepatic factor appeared to be entirely responsible, or to play an important part, in the fatal outcome. With a single exception, in which active hemorrhage was found, the outstanding postmortem findings in all of these cases were hepatic or hepatorenal changes, ranging from cloudy swelling to frank necrosis. Fatty metamorphosis was present in a number of instances, and in 3 was grossly evident. In the one patient in whom postoperative hemorrhage was the major cause of death, the liver was found at necropsy to be light grayish-brown and very soft, and the normal markings were absent. Microscopic examination revealed many small areas of necrosis, swollen hepatic cells and obliteration of the sinusoids. The patient died 12 hours after operation, and it seems reasonable to suppose that the hepatic changes had been caused by preoperative damage, aggravated by the falling blood pressure at operation (94/70) and the subsequent hemorrhage, with resultant anoxemia.

The most reasonable theory advanced to explain liver and liver-kidney deaths is as follows: Since any form of anesthesia has some effect on the liver, a certain fall in hepatic function can be expected after operation. The damage is accentuated by prolongation of the procedure and anesthesia, surgical trauma, blood loss and the toxic effects of tissue death. Furthermore, Crile has demonstrated that the opening of the abdomen alone causes a reduction of temperature in the liver and an accompanying decrease in chemical activity. Thus, a damaged liver, which is already the site of structural and functional alteration, may be so seriously affected by the above considerations as to become further damaged to a point where toxemia may be so overwhelming that so-called liver death occurs.

In preventing such deaths, the author suggests that even if functional liver tests are not practical routinely, preparation with diet, a liberal intake of carbohydrates and protein, and attention to the fluid balance could be carried out for 48 to 72 hours in ambulatory patients before hospitalization. Although the number of liver and liver-kidney deaths is small, it could be further reduced by such means.

(The so-called "liver death" apparently plays a definite, though relatively infrequent, part in the hazards of general surgery, and especially in the operative treatment of biliary tract disease. This is not surprising in view of the frequency of liver damage with gall bladder disease, especially when this involves the common duct and is associated with serious infection, obstruction of the duct and jaundice. That liver death may occasionally be encountered after gynecological surgery seems probable, as anesthesia in itself may be a causative factor. I do not believe, however, that a review of the deaths in any gynecologist's practice would reveal many in which the hepatic role is primarily concerned, although autopsy may often show secondary liver changes in patients who have died of severe infections, usually peritoneal. The simple precautions suggested by the author are sound enough, being those commonly advocated as a part of the pre-operative management where major abdominal procedures are contemplated.—Ed.)

## TIDAL IRRIGATION FOLLOWING GYNECOLOGICAL OPERATIONS

H. H. CUMMINGS AND R. K. RATLIFF

J. Michigan M. Soc., 45: 356-357, 1946

The authors describe a simple and inexpensive automatic bladder irrigator which has served with entire satisfaction following gynecological operations during the past 3 years. The apparatus is diagrammatically illustrated and the procedure outlined. It has been found that the cheapness of the irrigator permits a hospital to have sets of the apparatus available for all patients needing it. When properly set up and adjusted, the apparatus needs no further care than the refilling of the normal saline containers. The apparatus is claimed to be entirely satisfactory in the following respects: ease of operation, slight demands of nursing care, inexpensiveness, effectiveness of bladder drainage, and comfort of the patient. 1 figure.

## STERILITY

### SEMEN ANALYSIS IN 1500 CASES OF STERILE MARRIAGE

JOHN MACLEOD AND ROBERT S. HOTCHKISS

Am. Jour. Obstet., & Gynec., 52: 34-41, 1946

Examination of semen specimens in 1500 cases of sterile marriage showed that about 50 per cent had deficiencies either in spermatozoa count, motility or morphology. If we compare these figures with apparently normal standards in the literature we find, for example, that in a group of 200 men of known fertility, 25 per cent were found to have semen specimens with counts consistently below 60 million per cc. In another group of 100 apparently normal, young, unmarried men, the average spermatozoa counts were just slightly higher than those given for fertile, married men, and 22 per cent had spermatozoa counts consistently below 60 million. In these two groups, therefore, the average semen characteristics were remarkably similar. (J. Urol. 54: 474, 1945 and J. Clin. Endocrin. 3: 179, 1943.) In the sterile marriage series 618, or 41 per cent of the total number of men examined, had subnormal spermatozoa counts; and it is this group, not the completely sterile group with azoöspemia, which constitutes the main male sterility problem. Most of these men have normal histories and except in certain of the azoöspemias, no clean-cut etiologic factor has emerged to account for the considerable amount of male infertility recorded in this investigation.

As the spermatozoa counts falls below 60 million per cc., other defects such as motility and abnormal morphology, become more apparent until, in the very low count range, all three deficiencies together are likely to be found. It is suggested that 60 million per cc. spermatozoa count is a reasonable dividing line between good and impaired fertility.

In former years the 60 million line was drawn too sharply, and it was thought by a good many that men with counts below this mark were rarely fertile. Studies on men of known fertility have shown this view to be incorrect, and for initiating and pursuing this type of comparative study I believe that the authors deserve the chief credit. Their own suggestion, that a 60 million per cc. count is a reasonable dividing line between good and impaired fertility, represents a more conservative view than that above mentioned; since they, as well as other authors, have shown that fertilization is not rare with counts much lower than this. There has been considerable discussion as to the relative importance in prognosis of sperm counts and estimates of abnormal and immature forms, but the work of the authors indicate that there is more or less parallelism between these two factors, as well as that of mobility.

## THE PHOSPHATASE ACTIVITY OF HUMAN SPERMATOZOA

J. MACLEOD AND W. H. SUMMERSON

Federation Proc., 5: 67, 1946

The phosphatase activity of human spermatozoa has been determined manometrically and chemically in the presence of certain phosphate esters which are of known significance in the carbohydrate metabolism of other tissues. The substrates used were ATP, ADP, adenylic acid, the various hexose mono- and diphosphates, -glycerophosphate and acetyl phosphate. Because of the powerful and heterogeneous phosphatase activity of human seminal fluid, the results presented are based on the activity of spermatozoa washed several times to eliminate as much of the seminal fluid as possible.

In the presence of ATP, the spermatozoa showed a phosphate-splitting power equivalent to two-thirds of the total phosphorous of ATP. This would correspond to the formation of adenylic acid from ATP. Similarly, in the case of acetyl phosphate, the spermatozoa show a powerful phosphate-splitting activity.

The spermatozoa did not show any phosphate-splitting activity in the presence of any of the other phosphate esters studied though the seminal fluid and *once*-washed spermatozoa did produce considerable hydrolysis of *all* of them. Whether this is due to the inability of these substrates to penetrate the cell structure is not known.

The relation of these observations to the motile activity of the spermatozoa has also been studied.

EVALUATION OF A NEW CONTRAST MEDIUM  
FOR HYSTEROSALPINGOGRAPHY

J. B. MONTGOMERY AND W. LANG

Am. J. Obst. &amp; Gynec., 51: 702-705, 1946

The well-known shortcomings of various contrast media available for x-ray study of the uterus and uterine tubes have caused considerable restriction in the use of this valuable diagnostic procedure. Visco-Rayopake (diethanolamine salt of 2,4-dioxo-3-iodo-6 methyl tetrahydropyridine acetic acid), a new opaque medium which was introduced by Rubin in 1941, has been found to be highly satisfactory for x-ray study of the uterine tubes. This medium fulfills all of the following requirements: (1) adequate radiopacity, (2) rapid absorption, (3) freedom from chemical irritation, and (4) proper viscosity. Its outstanding advantage is that it is well tolerated by the tissues and is rapidly absorbed from the peritoneal cavity.

The authors used this substance to study the patency of the uterine tubes in 79 patients. In 25 of these, the Visco-Rayopake flowed freely into the peritoneal cavity where it was absorbed within 30 minutes. Excellent visualization of the tubes was made possible by the high viscosity of this medium.

## MISCELLANEOUS

### CERTAIN ASPECTS OF GYNECOLOGY AS RELATED TO GERIATICS

GEORGE W. KOSMAK

Clinics, 4: 1230-1249, 1946

The author discusses certain aspects of gynecology as related to geriatrics under the following headings: (1) general considerations; (2) disturbances and diseases of the external genitalia; (3) disturbances and diseases of the internal genitalia; and (4) therapy, medical and operative. Opinion may differ as to when "geriatrics" begins and whether or not the treatment of menopausal symptoms should be included in this presentation. While it may at times be necessary to refer to the later manifestations of the menopause, the author's discussion is limited largely to the disturbances which follow this period.

*General considerations:* The ovarian secretions, together with those from the pituitary, are essential to the proper functioning of the other sex organs. When secretion is inhibited or eliminated, whether during the gradual process of the menopause or by operative removal of the ovaries, senescence occurs in the tissues of the uterus, vagina, and their accessory structures, as well as the mammary glands.

However, the ovarian secretion is not the only factor which determines the transition from youth to age, and aging processes in the nervous, circulatory, digestive and urinary systems cannot be divorced from the gynecologic aspects. Therefore, the mere administration of estrogens fails to constitute a justifiable or satisfactory solution.

*Disturbances and diseases of the external genitalia:* The breasts are essentially dermal derivatives, and the subsidence of function is accompanied by structural changes in form and histology. They may become enlarged by the increase in fatty components or diminish in size due to a general atrophy. As the supporting ligamentous elements are stretched, sagging results and where opposing skin surfaces come in contact, irritation may develop into a local inflammatory process. The nipples may also become involved. The connective tissue may develop into nodular masses resembling possibly malignant growths. Other, not necessarily malignant growths, such as fibromata, adenomata and "milk cysts" may develop. In any suspicious cases, it is wise to resort to incision and biopsy. While mammary cancer as an initial lesion is more frequent at an earlier period and is more slow growing and of lesser malignancy at a later age, there is no time of life when it may not occur. Some investigators believe that excessive estrogen administration stimulates the production of malignancies in these organs, and this should be borne in mind by the practitioner.

Retgression of the vulva and vagina occurs with degeneration of the fatty

elements and a decrease in sensitivity of the nerve supply in these tissues. There is a consequent tendency to trauma and infection. The vulvar skin may become the site of such lesions as acute and chronic dermatitis, eczema, leukoplakia and kraurosis. A lack of cleanliness aggravated by a concentrated or highly acid urine contributes to produce local symptoms.

A variety of new growths, benign or malignant, may occur in the vulva and vagina. The former include sebaceous cysts, inclusion cysts, lipomata, fibromata, condylomata and rare growths such as tumors involving sweat glands and nerves. The malignant types are usually in the form of carcinoma of various types, sarcoma and melanoma. There are certain predisposing factors to the development of cancerous growths, chiefly leukoplakia, and also syphilitic lesions and warts. It is important therefore, that any complaint of irritation in the vulvar region be thoroughly investigated and a biopsy done of suspicious tissue areas.

The vagina likewise presents certain inherent disturbances: inflammatory, atrophic and neoplastic. Vaginal discharge may result in discomfort and irritation. A careful speculum examination should help in making a differential diagnosis between ordinary atrophic changes and neoplasms. Primary carcinomatous tumors are extremely rare, but may develop after the menopause, usually on the posterior wall or in the fornix. Secondary cancerous involvement of the vagina is more common and follows cervical or uterine cancer, after operation. Another tumor-like formation involves a protrusion of omentum or intestine through a weakened area in the vagina, and may follow constipation in older women.

*Disturbances and diseases of the internal genitalia:* The author draws attention first to the cervix. The chronic type of endocervicitis is frequently found in older women and may manifest itself by pelvic discomfort or secondary arthritis. In association with chronic inflammatory disease, cystic degeneration of the cervix is often found. Lacerations, the result of earlier injury, demand attention as they may be the starting point for later malignancies. Nearly 30 per cent of cases of cervical cancer arise after the age of 50. Although there is no definite train of symptoms, any return of bleeding after the menopause, however slight, should lead to speculum examination. Pain may not occur until the growth is far advanced.

Several varieties of uterine cancer are recognized: papillary, adenoma, adenoma malignum, glandular adenocarcinoma and solid carcinoma. Here again, postmenopausal vaginal spotting always calls for diagnostic curettage with histologic examination of the scrapings.

Ovarian neoplasms are very insidious, and periodic examination of all women after the menopause constitutes the most satisfactory procedure to avoid an unfortunate outcome since such neoplasms may give rise to very few and indefinite symptoms.

Other disturbances of the internal genitalia are uterine displacements and prolapse of the uterus. Urinary disturbances should also be considered because

of the close connection between the genital and urinary tracts in women. Urinary symptoms call for thorough investigation.

*Therapy, medical and operative:* Therapeutic measures for conditions in women who have passed the menopause cannot always be the duplicates of those applicable to earlier years. The selection of drugs and their effects needs to be considered very carefully and operative procedures must be judged by different standards. The author discusses the various therapeutic problems involved in the disorders described in this paper.

(Within recent years there has been increasing interest in the subject of geriatrics, and we now have a national association, with a national journal, devoted to its study and discussion. Geriatrics should include also a study of the factors involved in the processes of aging and senile decay, as well as the study of the diseases of old people, such as the long array of gynecological conditions so well discussed by Kosmak. These various diseases are merely manifestations of the aging process, the real causes of which are still not clear, although it brings about certain changes and changing predispositions in body tissues. —Ed.)

## THE LOCALIZATION OF EPIDEMIC PAROTITIS IN THE FEMALE GENITALIA

LUIGI DE GIORGI

Archivio di Ostetricia e Ginecologia, 51: 50-69, 1946

First, the author reviews in a not too critical fashion the bibliography on the subject. While the localization of the virus in the testes is very frequent, in certain epidemics which have spread among adults (soldiers, prisoners, etc.) as high as 100 per cent, the localization in the ovary is recognized by all as of extreme rarity. In only one epidemic, in a school for girls in Moscow, the oöphoritis was a more common complication (Troitski, 1906). A common sequel of orchitis is sterility. In the female we can neither deny nor affirm that the oöphoritis may in some cases cause sterility. A few cases were reported where sterility was secondary to a localization of the virus in the hypophysis, the clinical picture being one of pluriglandular insufficiency.

Menstrual disturbances, particularly metrorrhagia, are a frequent symptom in the cases of oöphoritis due to mumps. The author has studied, through a questionnaire, the after-effects of mumps on patients of the clinic and on his private patients. Of 4000 patients who suffered with mumps in only 600 did it occur near or after puberty. In the latter group, 6 patients complained of elevation of the temperature, pain in the lower abdominal quadrants and metrorrhasias 7 to 8 days after the swelling of the parotids. The patients recovered and as a rule all menstrual disturbances disappeared in a few months. In only 2 cases could the sterility possibly be attributed to mumps, but the concomitant presence of pleural adhesions in both cases makes the author believe that a tuberculous infection is a more likely cause.

The effects of epidemic parotitis in a pregnant female are still more difficult to establish. The occurrence of mumps during pregnancy is not very frequent. In spite of a number of cases that point to the benign nature of the infection to both mother and fetus, there are a few cases reported of abortions or premature deliveries that seem to have been caused by the virus infection. The author then presents a case of mumps in a pregnant woman. The patient, 38 years old, had previously had a normal pregnancy. About 3 months after becoming pregnant she suffered from an attack of mumps, both parotid glands being involved. The other symptoms were, fever (39°) for about 3 days, vomiting, headache and anorexia. Seven days afterward the temperature rose again, she complained of pains in the lower back and lower abdominal quadrants, and had free bleeding. She came then to the hospital and there expelled an embryo of 6 cm., recovering in a few days. Two months later she became pregnant again and had another normal pregnancy. Both her living children are alive and healthy. The examination of the placenta recovered (immediately after the patient expelled the embryo) by curettage has shown lesions of necrosis of the decidua basalis, with no abnormalities of the villi and chorion.

(The extension of mumps to the male gonad is relatively common, and its occurrence is readily demonstrable from the accompanying local signs. On the other hand, oöphoritis as a complication of mumps is exceedingly rare, and its occurrence is usually conjectural, because of the concealed situation of the ovaries. To employ menstrual disturbances or subsequent sterility as indices of such ovarian involvement would certainly be scientifically unsound, owing to the very great frequency of these conditions in women who have not had mumps. Even the occurrence of abortion in the pregnant woman with mumps does not justify the assumption that a specific oöphoritis has been responsible, for similar reasons. The author's study of this large number of cases is of definite value, chiefly because it emphasizes the rarity of this complication and the difficulties and uncertainties of diagnosis.—Ed.)

MARION SIMS AND THE "DENTAL JOURNAL": FIRST  
PUBLICATION BY THE FATHER OF GYNECOLOGY  
IN CHAPIN A. HARRIS' MAGAZINE

EUGENE J. MOLNAR

J. Am. Dent. A., 33: 601-609, 1946

The particular point of interest to gynecologists in this paper is that it refers to the very first medical paper of any kind written by Marion Sims, reporting a "double congenital harelip, absence of the superior incisors and their portion of alveolar process." It was published in the American Journal of Dental Science, 6: 51, 1844.



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# & *Obstetrics*

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## ABDOMINAL PREGNANCY\*

A REVIEW OF PRESENT KNOWLEDGE BASED PARTLY ON REPORTED CASES  
AND PARTLY ON THE EXPERIENCE OF THE CHARITY HOSPITAL OF LOUISIANA  
AT NEW ORLEANS DURING THE PERIOD JULY 1, 1937 THROUGH JUNE 30, 1945

BY W. D. BEACHAM, M.D., AND DAN W. BEACHAM, M.D.

*New Orleans, Louisiana*

From an historical viewpoint abdominal pregnancy is of particular interest because it was the first type of extra-uterine gestation to be recognized. Long before the classical picture of ruptured tubal gravidity was described, lithopedions and full term abdominal fetuses had been encountered and some of them actually removed. Occasionally these retained pregnancies became infected and formed abscesses which ruptured through the rectum, abdominal wall, vagina, or bladder, discharging pus and fetal parts. Others were discovered in various degrees of degeneration (most frequently calcification or mummification) at abdominal section, usually postmortem.

To "Albucasis (1013-1106), Abu'l-Qasim Khalef ibn abbas Al-Zahrawi, also known as Alzaharavius, who was born near Cordova, Spain, and is considered the greatest surgeon of the Mohammedan Renaissance," goes the credit for giving "the first reference to an intra-abdominal pregnancy in the form of a case report. He had seen a woman whose foetus had died without being expelled. She became pregnant the second time, and again the foetus expired. Some time later, the patient developed an umbilical abscess which ruptured, expelling a large number of small bones. She recovered, but the fistulous tract remained." Ricci, whom I have just quoted, expresses the opinion of many writers when he states that he is doubtful if any of the so-called Cesarean sections of the 16th century were authentic. He declares, "most of the reported cases on close analysis were instances of intra-abdominal pregnancies with or without fistula formation. Such perhaps was the case attributed to Jacob Nufer, the sow gelder of Sigerhausen in Switzerland, who operated upon his wife. It is said that despite the aid rendered by 13 midwives and several lithotomists, the patient failed to deliver. Nufer obtained permission of the city magistrates and forthwith incised the abdomen and delivered a living foetus. The woman also lived." The above was reported by Caspar Bauhin (1560-1624) in his editorial appendix to Francois Rousset's *Essay* which appeared in the 2nd edition of Wolff's *Gynaeciorum*.

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The incident is said to have occurred in 1500; Bauhin reported it in 1586. Cases of full term abdominal pregnancies were attributed to Achilles Pirminius Gasser (1505-1577), to Jean Joseph Courtial (fl. 1580) and Gilles Hertoghe of the 15th century. Colombat refers to this case in an edition of his text, quoting from *Exemp. Med. Observ.*, pp. 321-328, 1520.

We are told that prior to the 17th century practically all anatomical investigations were conducted on cadavers of executed criminals. Although Bartolomeo Eustachio (1520-1574) began to perform postmortem dissections, it was not until the following century that autopsy study brought to light a number of extra-uterine gestations including abdominal lithopedions and tubal pregnancies. James Primrose in 1595 included in his textbook on *Diseases of Women*, a remarkable case report of an abdominal pregnancy. The first pregnancy (intra-abdominal) produced a fistula in the lower abdomen which was enlarged and fetal parts extracted by Jacob Noierus. Two months later Stephanus Mainaldus deliberately incised the lower abdomen and delivered a second fetus.

One of the best early treatises on the subject of lithopedions and abdominal pregnancy was that by Laurent Strauss in his *Resolutio Observationis*, published in the 17th century.

The first authentic report of a case of tubal pregnancy with the classical symptomatology of rupture was recorded in 1616 by Riolan (1577-1657), according to Schumann and others. J. Astruc (1684-1765), who wrote a detailed treatise on the *Diseases of Women*, credited the first instance of ovarian pregnancy, observed in 1862, to de Saint Maurice. The first report of a case of a full term abdominal pregnancy was made in 1717 by Robert Houston. Charles Kelly gave the first description of a placental attachment in an abdominal pregnancy in 1763. During the 18th century there appeared a number of interesting case reports on tubal, abdominal, and ovarian pregnancies. Pierre Dionis gave the first clear description of cyesis in the uterine end of the tube in 1718.

The first gynecological operations performed in America were for abdominal pregnancy. John Bard, a New York surgeon, reported the case operated upon by him in 1759 in the *Journal of Medical Observations and Inquiries* 2: 369, 1762. The patient recovered. On January 14, 1791, and on February 6, 1799, William Baynham of Virginia, operated for the removal of an abdominal fetus, being successful in both cases. The third operation of this nature had been performed in the above interim by Charles McKnight. R. P. Harris, writing in 1887, stated that William Turnbull and Charles McKnight were the first to advise that the placenta be left in place in cases of this nature.

In 1876, the remarkable and comprehensive monograph on ectopic gestation by John S. Parry was published. The first operation for a ruptured ectopic pregnancy was performed by Lawson Tait in 1883. His writings are classical. The first operation performed for tubal pregnancy in America was done by Charles K. Briddon in the same year. In 1894 Werder surveyed the literature and found 16 successful cases of celiotomy for ectopic gestation with a living fetus at or near term. He reported such a case which he considered to be tubal pregnancy primarily. The malformed baby died on the 4th day, but the mother

recovered although "terrific hemorrhage" occurred at the time of operation. Sittner was considered to be one of the first authorities on the subject of abdominal gestation. In 1902, he reported 179 cases of advanced abdominal pregnancy. F. Schauta's collection of 241 cases was published in *Lehrbuch der Gesamten Gynakologie* in 1906. Beck studied the literature and sent questionnaires to over 200 obstetricians which caused him to report a study of 262 cases of extra-uterine pregnancy between the years 1809-1919, in which operations were performed after the 5th month with a living fetus. A bibliography was not presented.

The elucidative dissertation of Cornell & Lash appeared in the *International Abstract of Surgery* in August, 1933. It was based on a study of 236 cases, 226 from the literature and 10 of their own. They stated, "many case reports in the literature were incomplete. Nearly all mentioned what was done at operation, but in many of them other details which we desired to study were omitted. Not every case has been included in our review as some of the articles were inaccessible." They presented 22 tables.

In an article published in September, 1935, *American Journal of Surgery*, Hellman & Simon presented 9 pages summarizing the date of operation, operator, place of operation, result to mother, fetal result, and reference, of 316 cases of intra-abdominal pregnancy. They reported one case of their own, in which mother and baby lived. They included all of Sittner's cases even though in his series fetuses of 22 weeks gestation were included, but since 1906 they put into the series only cases in which the fetus was of at least 28 weeks gestation. In their total study of 316 cases, the fetus lived in 158. By "lived" they mean "survived 8 days or longer." Two hundred and twelve mothers lived, 101 expired, and the outcome in 3 was unknown. They stated, "In the whole series there are only 80 cases in which both mother and child survived and of these 80, it is probable that the mother and child were not entirely well in more than 50. This figure is not arrived at by any true statistical study but rather by the impression one gets from the review of hundreds of these cases." Of the 316 cases the fetus was removed *via vaginam* in two and the rest were extirpated by laparotomy. They found 2 cases of combined intra-abdominal and intra-uterine pregnancy. In both cases the mother and infant survived. Gardner & Middlebrook in the November, 1944, *American Journal of Surgery*, discussed "Abdominal Pregnancy" and stated, "In this paper we propose to add 22 more well reported cases from the literature to the analysis of Cornell & Lash, bringing the total up to 258, and to report a case of the rarest type of abdominal pregnancy—a full term, surviving infant without congenital anomalies or deformities and a surviving mother." The baby weighed 4 pounds, 15 ounces. He died of pneumonia at 4½ months. The mother expired 2 years subsequently of metastasizing carcinoma of the breast.

Inasmuch as there was no complete diagnostic or cross index system in the record library at the Charity Hospital of Louisiana at New Orleans prior to July 1, 1937, it was deemed advisable to begin this study with the first case admitted after that date, which also was the beginning of the residency of the

senior author there. Some of the more recent cases were managed during the residency of the junior author before his leave-of-absence for military service. As designated by the history numbers, these cases have been supervised by the Tulane University, Louisiana State University, or Independent Units; consequently, we are indebted to the Chiefs of those services and the members of their respective Staffs for the privilege of discussing them. This series of 20 instances of abdominal pregnancy treated during the 8-year period ending June 30, 1945, does not include an ovario-abdominal gestation case (T-38-61487) due to the fact that the fetus had been absorbed before the patient was laparotomized. Obviously, we have excluded from this discussion the large number of "old ruptured ectopics" which have been admitted to the New Orleans Charity Hospital believing that one should not diagnose a case as being one of abdominal pregnancy unless the fetus is actually living in the abdominal cavity or unless there are definite evidences that it has lived there.

#### INCIDENCE

##### *Race*

In the interim under consideration there have been 41,634 deliveries (11,419 white and 30,215 colored) and 394 cases (155 white and 239 colored) of ectopic gestation, excluding the abdominal and ovarian types, at the Charity Hospital in New Orleans. The total incidence for the 8-year period would be one to 2,081 deliveries. For the white race the figure would be one to 11,419 deliveries, while over this short period of time the colored ratio was one to 1,685 deliveries. Checking the general incidence of extra-uterine pregnancy (with the above mentioned exceptions) the figure is one ectopic case to 106 deliveries. The ratio for the white obstetrical service is one to 73 and for the colored one to 126. One would conclude from these figures that the colored persons in the vicinity of New Orleans are more apt to procrastinate coming to the Hospital where many of them would be treated surgically as tubal abortion and ruptured ectopic pregnancies and thereby prevent them from becoming abdominal gestation cases.

Harrar in a study of 10 cases (3 of which were previously reported by Davis & Jellinghaus) in 1927, recorded an incidence of one in 15,600 confinements at the New York Lying-In Hospital. Colvin & McCord found 16 cases of secondary abdominal pregnancy of 5 months or more in 12,000 cases admitted to the colored division of Grady Hospital (Atlanta, Ga.) from 1924 to 1933. In 275 cases in which the race was mentioned in the literature, we found 173 whites, 81 Negro, and 21 others (Table 1). In reports since 1930 we have noticed a predominance of colored persons.

##### *Age*

In this group the youngest was 18 years of age and the eldest 37, which figures coincide with those of the contributors just mentioned. The majority of this Charity Hospital series were between 25 and 35 years of age. In this connection it is interesting to note that 88 cases found in the literature mentioning age were

above 35 years (Table 2). Writing in 1922, Graffiagnino reported 11 cases of advanced extra-uterine pregnancy which were managed at the New Orleans Charity Hospital from 1906 to 1920. Included was a negress of 90 years who experienced the menopause at 40 years. She expired in the hospital and at autopsy a calcified well defined fetus was found in the left adnexal region, the fallopian tube having been completely obliterated.

### *Gravidity*

As shown by Table 3, and as would be expected, a great proportion of the patients have been previously pregnant. Periods of sterility or infertility have

TABLE 1  
*Abdominal pregnancy—racial incidence*

	REPORTED CASES	N. O. CHARITY HOSPITAL SERIES	TOTAL
White.....	173	1	174
Negro.....	81	19	100
Other.....	21	0	21

N.B.: Unfortunately the race was not mentioned in a large per cent of the reports.

TABLE 2  
*Abdominal pregnancy—age incidence*

YEARS	REPORTED CASES	N. O. CHARITY HOSPITAL SERIES	TOTAL
15-19	7	1	8
20-24	33	2	35
25-29	61	6	67
30-34	67	6	73
35-39	67	5	72
40 plus	21	0	21

Lithopedions were found in persons of 55, 64, 90 and 94 years. In many instances in the literature age was not stated.

been mentioned by some of the writers, notably Lane, Brown, Reel & Lewis, Kauffman, and Finley & King.

### ETIOLOGY & PATHOLOGY

When studying the literature one cannot fail to be impressed by the controversy regarding the occurrence of primary abdominal pregnancy, in which instance the ovum is fertilized while free in the peritoneal cavity and implants itself on the peritoneum. A number of writers, including Goodpasture, Ray, Maxwell, Furgason, Best, Tomasi, Studdiford, Thomas, and Weiner, have reported cases which seem to qualify as such; however, many of the contributors are not certain that an impregnated egg can implant itself on the peritoneum and live. They

contend that careful retrospective analysis of the histories of abdominal gestation patients usually elicits a positive diagnosis of tubal cyesis in which the products of pregnancy ended up in the abdomen after rupture of the salpinx or the occurrence of an abortion by the tube.

In 1932, E. L. King directed our attention to a very rare cause of extra-uterine gestation, viz. postoperative separation of the uterine incision of a cesarean section. He reported 4 such cases, in 3 of which the ovum had implanted itself upon the omentum attached to the abdominal wall. He believes that the fertilized ovum escaped through the uterine mural defect and became implanted as a primary abdominal pregnancy in each of these cases. Dr. King emphasizes that this condition must not be confused with rupture of a uterine section scar. All of us know that in the latter we may expect disastrous fetal and maternal results if the rupture is complete and treatment is not instituted very promptly—a fact pointed out in an analysis of 64 cases of ruptured uteri managed at the New Orleans Charity Hospital. Geppert reported a case of antepartum rupture

TABLE 3  
*Abdominal pregnancy—gravidity incidence*

GRAVIDA	REPORTED CASES	N. O. CHARITY HOSPITAL SERIES	TOTAL
I	69	8	77
II	82	6	88
III	36	1	37
IV	26	2	28
V	11	0	11
VI	12	3	15
VII	9	0	9
VIII	1	0	1
IX plus	8	0	8

of the uterine scar following low flap cesarean section and giving rise to a "secondary abdominal pregnancy."

From a study of the recorded knowledge about this question and the actual findings in the 20 cases here considered, we have concluded that all of the latter were of the secondary abdominal type, for the designation of which some of the writers prefer the term *advanced ectopic pregnancy*. To further emphasize the value of a carefully obtained detailed history we might say that the case of E. C. (I-39-14116) could have easily been mistaken as an instance of primary abdominal pregnancy inasmuch as the placenta was attached on the posterior aspect of the uterus and both salpinges were patent. The history was compatible with a tubal abortion. Just how often tubal abortion with resultant death of the fetus takes place, we are at a loss to know. Similarly, we do not know how many tubal pregnancies undergo spontaneous regression and pass unnoticed although we have excellent reason to believe that there is a goodly number of such. Likewise, only a relatively small per cent of the cases of ruptured salpingal gestation become abdominal pregnancy cases. The condition

of the fetus and the amount of bleeding at the time of rupture are two of the main factors which govern the continuation of the pregnancy.

Schumann described a very unusual case of a tubal pregnancy which reached term. There are a number of instances of intraligamentary pregnancy in the literature. Two such cases which reached term were reported by Ware in 1934. In 1926 Novak found 276 cases of combined extra-uterine and intra-uterine pregnancy in the literature. Of these there are 9 instances in which both intra-uterine and extra-uterine fetuses are recorded as having gone to term and been delivered alive. Wilson reported such a case in 1880, the first baby being born *via passages naturales* at 8 months and the second being delivered at term by laparotomy. Lull & Bernstine, and Harrar have reported a case of twin abdominal pregnancy. McMillan & Dunn described a case of abdominal pregnancy following supracervical hysterectomy. Ovarian pregnancy, rare as it is, may give rise to cyesis of the secondary type.

One thing is certain, namely, that the entire life cycle of an abdominal pregnancy is abnormal, a fact emphasized by Wharton. The placenta with its trophoblastic activity becomes attached to and attacks any structure with which it comes in contact. It is no wonder then that we may find it incorporated with different organs including the uterus, tubes, ovaries, omentum, colon, rectum, ileum, appendix, cecum, jejunum, bladder, stomach, gallbladder, liver or spleen. Obviously, a serious surgical problem may exist when one considers removal of such a placenta and not infrequently it is good surgical judgment to refrain from attempting to remove it.

The fetus and its membranes may become adherent to the peritoneum and any of the intra-abdominal structures. After fetal death, absorption, calcification, mummification, skeletonization, or infection occur. Sloughing of fetal parts from the abdomen may eventuate. In many reported instances the fetus reached term and was delivered by abdominal section. The total number of reported cases of abdominal pregnancy operated upon at or near term with a living mother and baby is large. Much larger, however, is the group in which the fetus was dead. The number of mothers and/or fetuses which have died without having been reported is probably the largest.

#### SIGNS & SYMPTOMS

As may be seen in Table 4, the history of previous gestations is not particularly informative. In the present pregnancy, after the 4th week, abdominal pain, weakness, nausea, vomiting, or syncope may have occurred, indicating tubal abortion. The symptoms are usually increased if rupture occurs and will be governed very largely by the condition of the patient and the extent of bleeding, which in turn is dependent upon the location of the sites of implantation and rupture. Many of these women have had bleeding *via vaginam* which they term "spotting." (Table 5.) Some of them have passed a decidual cast. The intelligent ones seek medical counsel because of such symptoms and are properly given the benefit of surgery. If operation is not performed the odds are that the fetus expires and the products of gestation are absorbed or form a pelvic

hematocele. On the other hand if the fetus lives, the pregnancy continues abdominally with certain characteristic features which usually appear in the course of time. Among the latter are abnormal lie of the fetus, abnormal fetal movements, and abnormally loud fetal heart tones. When the fetus has reached  $4\frac{1}{2}$  or 5 months the patient may notice that movements are increased and more bothersome than has been the case with previous pregnancies. As time elapses this complaint is apt to be aggravated. Furthermore, the mother is often conscious of the fact that the baby is quite high or in a transverse lie. As will be subsequently pointed out, the examiner may note superficiality of fetal parts

TABLE 4  
*Abdominal pregnancy—character of previous gestations*

PREVIOUS PREGNANCIES	REPORTED CASES	N. O. CHARITY HOSPITAL SERIES
Term only.....	118	6
Term and abortion.....	21	1
Abortion only.....	28	1
Term, abortion and ectopic.....	1	0
Term and ectopic.....	2	0
Ectopic only.....	2	0
Abortion and ectopic.....	1	0
Not reported as to type.....	88	4
Premature labor.....	1	0

Eight of the N. O. Charity Hospital Group were primigravidas.

TABLE 5  
*Abdominal pregnancy—history of bleeding*

TYPE	REPORTED CASES		N. O. CHARITY HOSPITAL SERIES	
	Early	Late	Early	Late
Spotting.....	37	6	7	1
Continuous, mild.....	12	17	1	0
Irregular.....	20	22	2	0
Clots.....	3	6	1	0
No bleeding.....	8	—	2	—

either abdominally, rectally or vaginally due to the fact that there is no uterine musculature between the examiner's fingers and the fetus. In many instances distended intestines are responsible for the absence of the above mentioned classic findings just as they may prevent one from eliciting unusual loudness of the fetal heart tones.

If term is reached, a short pseudo-labor with inconsequential "pains" may occur. Three of the cases here reported were certain that they were "in labor." Brown, Cullen, Holden, and many others have observed similar ones. Fetal death and degeneration of the placenta may come about. After expiration of the fetus, loss of appetite, malaise, weakness, increased constipation, and fever

are the rule. A loss of weight may occur. Uterine bleeding is apt to be noticed. If fetal activity has been experienced the patient reports that she no longer feels the baby move.

#### DIAGNOSIS

If the patient is in the first half of pregnancy one may encounter considerable difficulty in proving the diagnosis of abdominal pregnancy. After obtaining a detailed history, one should carefully examine the patient from the top of the head to the soles of her feet. The mask of pregnancy may be present. The breasts may be enlarged and pigmented. The thyroid gland may be physiologically enlarged. The abdomen may be of an abnormal shape; it may be tympanic; and an abnormal mass may be palpable. Vaginal examination is apt to disclose discoloration of the mucous membrane of the vagina and cervix. Softening of the cervix uteri is usually not pronounced and that structure is commonly not dilated. Effacement is absent. Movement of the cervix is expected to cause pain. It may be displaced. A mass, boggy or pulsatile, may be palpable in the cul-de-sac or either adnexal region. The corpus uteri may or may not be satisfactorily outlined by palpation. The physician is thus confronted with the problem of making a differential diagnosis and he will consider the following: threatening or threatened abortion of intra-uterine pregnancy, incomplete uterine abortion; "missed" uterine abortion; ectopic (most commonly tubal) gestation, intact, with abortion, or with rupture; pelvic inflammatory disease; uterine tumor; ovarian tumor; or endometriosis. If the pelvis is "frozen" one must also include a consideration of the possibility of malignancy or tuberculosis or old ruptured ectopic. One must decide regarding the advisability of cul-de-sac puncture, testing of patency and dilatability of the cervical canal, and hysterosalpingography. A Friedman-Lapham test may be indicated, although too much reliance must not be placed on a "negative" result. The value of cul-de-sac puncture in diagnosing cases of ectopic gestation with intra-abdominal hemorrhage has been emphasized by Conrad Collins, Perry Thomas, and Schauffer. Culdoscopy may be indicated in certain cases of unruptured ectopic gestation.

If the pregnancy has advanced beyond  $4\frac{1}{2}$  months, diagnosis should not be so difficult provided one investigates the case with the possibility of abdominal pregnancy in mind. In addition to the above mentioned findings one may be fortunate enough to note that the fetus is in a transverse lie. Such a fetal position in a primigravida should be considered evidence of abdominal cyesis until the contrary is proved (Fig. 1). In this Charity Hospital series it was observed 3 times. In multiparae it may also mean extra-uterine gestation or may be due to relaxed uterine muscle, an obstructing tumor, polyhydramnios, multiple pregnancy, or fetal abnormality. In some instances the fetus is "high" (Fig. 2), but in others it may be in such a position that the usual pelvicephalograms would not prove it to be outside of the uterus. Such was the situation in our Case III (I-39-14116) whose x-ray film photograph is shown (Fig. 4). Abdominal tenderness is the rule in cases of gestation in the abdomen and it may be present to

hematocele. On the other hand if the fetus lives, the pregnancy continues abdominally with certain characteristic features which usually appear in the course of time. Among the latter are abnormal lie of the fetus, abnormal fetal movements, and abnormally loud fetal heart tones. When the fetus has reached  $4\frac{1}{2}$  or 5 months the patient may notice that movements are increased and more bothersome than has been the case with previous pregnancies. As time elapses this complaint is apt to be aggravated. Furthermore, the mother is often conscious of the fact that the baby is quite high or in a transverse lie. As will be subsequently pointed out, the examiner may note superficiality of fetal parts

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time it may be noticed that the cervical canal cannot be dilated as easily as in normal pregnancy.

"Soft tissue" technique x-ray films may give valuable information as pointed out by Mattingly & Menville, who cite the work of Snow & Powell, and Brown & Dippel. Such radiographic studies not only may show evidences of fetal death if expiration has occurred but also may give good indications that the fetus is outside of the uterus.



FIG. 2. Roentgenogram showing high location of the fetus (Case I)

In 1914 Cary published his article pertaining to hysterosalpingography; however, it was 11 years later when Bermann first injected iodized oil into the uterine cavity for the purpose of verifying a diagnosis of abdominal pregnancy, according to Gabaston & Harguindeguy. Since then the importance of hystero-graphy in diagnosing abdominal gestation has been pointed out by Mendenhall; Couvelaire, Portes & Digonnet; Titus & Eisaman; Colvin & McCord; Friedman; Harris; Kobak; Mattingly & Menville; Muckle; Osborn; Swanson; and Greenhill. We know of no pregnancies that have been interrupted at the New Orleans Charity Hospital by the instillation of radio-opaque substances into the uterus for the purpose of obtaining uterograms or hysterosalpingograms. Our experience with

such a degree as to interfere with palpation of fetal parts or fetal movements in some instances. Likewise distended intestines may cloud the picture and also prevent fetal heart tones from being easily heard. Too much emphasis cannot be placed on the vaginal, vagino-abdominal, and recto-vagino-abdominal examinations in these cases. The cervix uteri is usually displaced, the displacement being largely governed by the location of the fetus. It is often found



FIG. 1. Roentgenogram showing transverse lie of the fetus (Case IX)

behind the symphysis pubis and may require some little effort to visualize it. It is usually soft; sometimes very soft. Dilatation may be present but it is unusual for it to be greater than 2 cm. unless someone has been guilty of dilating it. Effacement is notably absent even in those cases who are having or have had pseudo-labor. One is fortunate indeed to be able to outline the uterine fundus in these cases. Some of them are best examined under anesthesia or saddle spinal analgesia. The round ligaments are impalpable as contrasted with their cordlikeness in normally advanced pregnancy. Palpation of the cul-de-sac contents may reveal superficiality of fetal parts. If the case is near or at term the finger may be used to determine the emptiness of the uterus. At that

hope that the placenta can then be removed with safety, appears in the light of an exhaustive analysis by Gordon Ley of 100 cases of advanced extra-uterine gestation, to be wrong."

Several considerations enter into the decision as to whether the placenta should be removed. Obviously, one is its location. In many of the reported cases, just as in some of this Charity Hospital series it was easily removed without appreciable loss of blood. If the fetus is alive or has only recently expired and the blood supply of the placenta cannot be ligated because of its location, then, as Litzenberg stated, "attempts to remove the placenta are exceedingly

TABLE 6

*Abdominal pregnancy—pre-operative diagnoses in 243 abdominal gestation cases*

DIAGNOSIS	REPORTED CASES	N. O. CHARITY HOSPITAL SERIES
Abdominal pregnancy.....	109	15
Normal pregnancy.....	31	0
Pregnancy and fibroid tumor.....	20	0
Pregnancy and ovarian cyst.....	20	0
Placenta previa.....	7	0
Abortion.....	6	0
Pregnancy and acute appendicitis.....	5	0
Pregnancy and intestinal obstruction.....	4	0
Pregnancy and pelvic infection.....	3	0
Pregnancy and premature separation of the placenta.....	3	0
Pregnancy with transverse presentation.....	2	1
Pregnancy and cervical obstruction.....	2	0
Pregnancy and proclivencia.....	2	0
Ruptured uterus.....	2	0
Pregnancy and toxemia with contracted pelvis.....	1	1
Pregnancy and gallbladder disease.....	1	0
Pregnancy and peritonitis.....	1	0
Dead fetus with toxemia.....	0	1
Ectopic pregnancy with bleeding.....	1	1
Pelvic tumor and peritonitis.....	1	0
Metritis.....	1	0
Polyhydramnion with dead fetus.....	0	1
Many diagnoses.....	1	0

dangerous." Kerr mentions "separation of the sac by degrees and carefully 'understitching' bleeding points," but here again it would be better to leave well enough alone. One thing is certain: it is better to have a living patient with a placenta left in the abdomen than it is to have a dead one whose demise can be attributed to hemorrhage due to the unfortunate removal of an unfavorably located placenta. If it does not become absorbed as is the general rule, then it can be surgically removed at a later date.

Instances of a second operation required for the removal of a placenta left in the abdomen have been reported by Beck, Lull & Bernstine, Renner, Rauch, Nicodemus & Craig, and Pearson. When a decision is made to leave the placenta in place as it was in 2 of the New Orleans Charity Hospital cases and many times

the use of skiodan and gum acacia solution is such that we highly recommend it. In our enthusiasm for hysterosalpingography we do not wish to give the impression that it should be performed indiscriminately or improperly; however, we agree with Greenhill that "in the presence of a dead baby the procedure is practically harmless." Colvin & McCord attributed one death to pulmonary embolism following faulty technique. In this Charity Hospital series only 2 cases were subjected to uterographic investigation although 16 cases had other types of x-ray studies, chiefly plain K.U.B. films.

For the sake of completeness a few words must be devoted to laboratory data in abdominal gestation cases although they are of little aid in making a diagnosis with the exception of the Friedman-Lapham test and in some cases it is of minimal or no help. If that test is positive it means that pregnancy or one of the hormonal pregnancy-like states exists. Obviously it does not give information pertaining to the location of the fetus. And, as has been pointed out by Novak, Curtis, Titus, DeLec & Greenhill, Posner, Reel & Lewis, a negative Aschheim-Zondek or Friedman-Lapham test must not be relied upon in arriving at a diagnosis of extra-uterine pregnancy including the abdominal type. Leukocytosis is the rule but there is nothing diagnostic about it. Likewise anemia and rapid blood sedimentation rate can be expected, any hemorrhage causing a further aggravation thereof. The urine was concentrated in most of the New Orleans Charity Hospital group.

The pre-operative diagnosis in the reported series and in the Charity cases are shown in Table 6.

#### TREATMENT

We share in the generally accepted opinion of the many contributors to the literature that laparotomy should be performed as soon as the diagnosis is made unless the pregnancy is near term and the fetus is alive, in which event operation may usually be postponed until approximately the 36th week provided the general condition of the mother is good and she is kept under observation as a hospital patient. As Titus has stated, "this risk must be fully explained to her and her husband." He also points out that the patient's religious adviser, if properly informed, can usually assist the patient in deciding to be hospitalized. Curtis expressed the belief of one group when he wrote, "In general, operation is indicated as soon as a diagnosis of advanced extra-uterine pregnancy has been made. The desire for a living child is no consideration; continuation of life until the period of viability is rare; and those babies which live may be expected to be hopelessly crippled or deformed."

In the words of Berkeley & Bonney "The whole question of the operative treatment of advanced extra-uterine gestation (7th, 8th, and 9th months and after term) is beset with great difficulties, the more so since the cases are so rare that no individual operator has had sufficient experience to enable him to generalize, while the conditions found are so different in their anatomy that no 2 cases are alike. The treatment formerly recommended, namely, that of postponing operative interference until the child has been dead some time, in the

## NEW ORLEANS CHARITY HOSPITAL SERIES

Inasmuch as we have presented data regarding color, age, gravidity, character of previous pregnancies, etc., in tabular form, we herewith wish to report very briefly, chiefly for purpose of record, the 20 cases comprising the series managed between July 1, 1937 and June 30, 1945, inclusive.

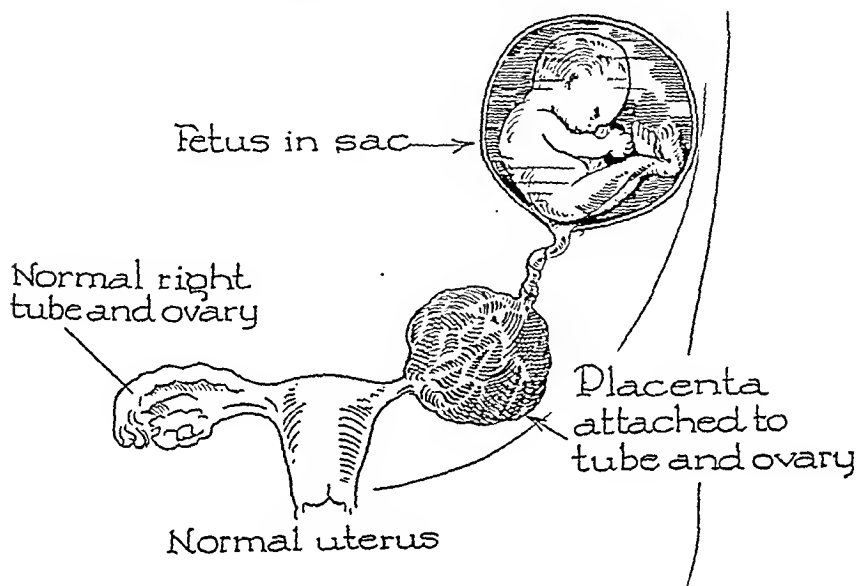


FIG. 3. Abdominal Pregnancy following Tubal Rupture. Sketch revealing placental attachment to left tube and ovary in Case I

I. H. J. (T-37-15027), married, G. VI, P. IV, was admitted on 10/7/37 with a chief complaint of pain in the abdomen. LMP occurred in May. History compatible with tubal rupture the last of July. B.P. 100/75; T. 100; P. 115; R. 28. Mass palpable in the left adnexal region. Uterine bleeding was present. Movement of the cervix caused pain. X-ray film of the abdomen revealed the presence of an extra-uterine fetus, high in the abdomen, as shown by Figure 2. Hgb. 70%; R.B.Cs. 3,625,000; W.B.Cs. 17,750. After receiving 2 transfusions, she was laparotomized under inhalation anesthesia, 10/9/37, and a fetus of approximately 5 months removed. See Figure 3. It showed evidences of having expired about 1 week previously. A left salpingo-oophorectomy was performed removing the placenta in toto. Operation performed by W. D. Beacham and C. G. Collins. The postoperative convalescence was uncomplicated and the patient was discharged on 10/21/37.

II. J. M. N. (L-39-4498), M.-S., G. II, P. I, was admitted 1/26/39 with the chief complaint of pains in the abdomen. LMP in November, 1938. History compatible with tubal abortion in December. B.P. 124/70; T. 101.2; P. 128; R. 36. Generalized abdominal tenderness. Mass in R.L.Q. X-ray film obtained January 30 revealed evidences of a dead extra-uterine fetus. Hgb. 60%; R.B.Cs. 1,100,000; W.B.Cs. 17,000. On March 8 under inhalation anesthesia, laparotomy performed by P. Graffagnino and H. Leidenheimer. The purulent products of pregnancy were removed and the abdomen drained. Patient was discharged with a draining wound on 4/11/39.

III. E. C. (I-39-14116), married, G. VI (youngest child born in 1934) was admitted 3/27/39 with a chief complaint of "peculiar pains" in the abdomen. LMP July, 1938.

in the literature, the cord should be ligated short and the abdomen closed without drainage. Only in the presence of infection need chemotherapeutic agents, such as one of the sulfonamides, be introduced into the abdomen. Marsupialization may be recommended in the presence of infection, but most of those men who mention it condemn the procedure.

The subject of the hormonal influence of the abdominally retained placenta has received the attention of Ware & Main, Hoffman, MacGregor, and others.

Blood transfusions play a major role in the successful management of abdominal gestation cases. Anemia is a common finding; consequently, many cases require pre-operative transfusions as well as postsurgical ones. It is

TABLE 7  
*Abdominal pregnancy—age of fetuses and fetal results*

	REPORTED CASES	N. O. CHARITY HOSPITAL SERIES
2-3 months.....	9	0
4-5 months.....	27	7
6-7 months.....	20	3
8-9 months.....	44	0
Over 10 months.....	2	0
Died.....	92	18
Lived.....	18	2

TABLE 8  
*Abdominal pregnancy—placental management and maternal mortality*

PROCEDURE	REPORTED CASES	DEATHS	N. O. CHARITY HOSPITAL SERIES	DEATHS
Placenta removed entirely.....	172	17	16	0
Placenta removed partially.....	15	2	1	0
Placenta left entirely.....	61	11	2	0
Not reported.....	44	3	0	0

surely a mistake to open the abdomen of one of these patients without having compatible blood immediately available. Shock must be prevented. The extent of the surgery to be performed will be governed by the findings. Obviously, nonpathological structures should not be removed, while on the other hand diseased internal genitalia should be extirpated. Decision regarding the advisability of prophylactic appendectomy must be made in each case. Post-operatively one must be prepared to treat abdominal distention and to improve the general condition of the patient as rapidly as possible.

The age of the fetuses at the time of operation together with their outcome is shown in Table 7, while Table 8 reports maternal mortality correlated with placental management.

infusion. A postmortem section revealed the presence of a 6 pounds, 9½ ounce fetus with a club-foot and deformed jaw. Generalized peritonitis and a right pyosalpinx were present.

VI. P. D. (T-39-34941), married, G. IV, was admitted on 7/27/39 complaining of pain in the abdomen and absence of fetal movements for approximately 2 weeks. LMP October, 1938. History compatible with ruptured tubal pregnancy in December. T. 101.4; P. 122; R. 35. Uterograms confirmed the diagnosis of abdominal pregnancy with radiographic evidences of fetal death. Hgb. 75%; W.B.Cs. 7,100. Under inhalation anesthesia, laparotomy was performed July 29 by K. Havard and G. A. Varino. Fetus showed evidences of maceration. Placenta was removed without difficulty. Transfusions were given and the



FIG. 5. Case III specimen showing placental attachment to uterus

patient's postoperative course was uncomplicated except for an upper respiratory infection. She was discharged in good condition on 8/10/39.

VII. E. P. W. (T-40-41002), married, G. III, was admitted on 8/16/40 complaining of pain in right lumbar region. LMP January 1940. History of "feeling bad" since onset of pregnancy. Appetite poor. Loss of 20 pounds in weight in 6 months. B.P. 120/80; T. 99; P. 90, R. 20. Abdominal enlargement compatible with pregnancy. Fetal heart tones not heard. Uterus enlarged to the size of a 2 months gravid state and displaced to the left by a mass on the right side. Under inhalation anesthesia, patient laparotomized 8/24/40 by C. G. Collins and J. Jones, a macerated fetus being obtained. Bilateral salpingo-oophorectomy, supracervical hysterectomy, and appendectomy were performed, all placental tissue being removed, inasmuch as it was attached to the uterus and right tube and ovary. Stilbesterol was given for postoperative breast pain. Patient was discharged 9/6/40 in good condition.

VIII. C. B. (T-41-4330), married, primigravida, was admitted 1/24/41 complaining of tenderness over entire abdomen. History compatible with tubal abortion in August, 1940.

History compatible with tubal abortion in August. B.P. 158/100; T. 98; P. 80; R. 24. Fetal movements absent for 7 weeks. The thyroid is palpable. Tenderness in lower abdomen. Cervix is hard and directly behind the symphysis pubis; marked bulging in the cul-de-sac with superficiality of fetal parts. Movement of cervix caused pain. Roentgenograms gave evidence of fetal death (Fig. 4). Diagnosis of abdominal pregnancy made. Hgb. 55%; R.B.Cs. 3,200,000; W.B.Cs. 6,000. Laparotomy performed March 30 under inhalation anesthesia by W. D. Beacham and G. A. Varino. Fetus was a 7½ months macerated female. Placenta was found attached to the posterior aspect of the uterus. See Figures 5 and 6. Bilateral salpingo-oophorectomy and total hysterectomy performed. Transfusions were given. Postoperative course was complicated by severe pharyngitis. Patient discharged on 4/23/39 in good condition.



FIG. 4. A.P. roentgenogram of Case III showing cephalic presentation, with collapsed cranial vault

IV. M. T. (T-39-33059), married, G. VI, P. V (youngest child being 1½ years), was admitted 7/17/39 complaining of inability to rest and excessive fetal movements. LMP in September, 1938. History compatible with tubal rupture in November. Size of abdomen compatible with term pregnancy. B.P. 120/86; T. 98.6; P. 90; R. 26. Cervix undilated. Laparotomy performed 7/18/39 under inhalation anesthesia by G. A. Mayer and G. A. Varino. A well formed 7 pounds, 13 ounce living fetus delivered. Placenta was removed without difficulty. Transfusions given. Postoperative convalescence uncomplicated. Patient discharged 7/31/39.

V. B. P. (T-39-13548), married, primigravida, was admitted on 3/23/39 complaining of marked pain in the abdomen. LMP 7/9/38. B.P. 102/78; T. 98.6; P. 90; R. 25. Abdomen extremely tender. Fetus in a transverse lie. Cervix soft and in normal position. Movement of the cervix caused pain. The diagnosis of extra-uterine pregnancy was completely missed and inductions of labor were attempted. Hgb. 45%; R.B.Cs. 3,000,000; W.B.Cs. 8,000. On 4/1/39 the temperature reached 101. That night she expired while receiving an

infusion. A postmortem section revealed the presence of a 6 pounds, 9½ ounce fetus with a club-foot and deformed jaw. Generalized peritonitis and a right pyosalpinx were present.

VI. P. D. (T-39-34941), married, G. IV, was admitted on 7/27/39 complaining of pain in the abdomen and absence of fetal movements for approximately 2 weeks. LMP October, 1938. History compatible with ruptured tubal pregnancy in December. T. 101.4; P. 122; R. 35. Uterograms confirmed the diagnosis of abdominal pregnancy with radiographic evidences of fetal death. Hgb. 75%; W.B.Cs. 7,100. Under inhalation anesthesia, laparotomy was performed July 29 by K. Havard and G. A. Varino. Fetus showed evidences of maceration. Placenta was removed without difficulty. Transfusions were given and the



Fig. 5. Case III specimen showing placental attachment to uterus

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VIII. C. B. (T-41-4330), married, primigravida, was admitted 1/24/41 complaining of tenderness over entire abdomen. History compatible with tubal abortion in August, 1940.

B.P. 130/68; T. 98.6; P. 85; R. 26. Findings compatible with pregnancy of approximately 6 months, the fetus being in a transverse lie. X-ray films disclosed evidences of fetal death. Under inhalation anesthesia, a macerated fetus was removed 1/31/41 by E. L. King and J. H. Herring. A mass consisting of placental tissue was found in the left adnexal region but was not disturbed. Patient's course was satisfactory and discharged on 2/10/41.

IX. M. C. (L-41-19217), married, G. I., admitted 10/31/41 with a complaint of continuous vomiting and contractions of every 5 minutes lasting about 30 seconds, with slight bleeding via vaginam. LMP 12/27/40. History is compatible with tubal rupture in April, 1941. B.P. 168/104; T. 100; P. 120; R. 30. Marked tenderness of the abdomen. Fetal heart tones not heard. The cervix admitted only one finger and the uterus found to be very firm.



FIG. 6. Case III specimen showing size of uterus

X-ray films were compatible with abdominal pregnancy, the fetus being in a transverse lie (Fig. 1). Hgb. 70%; R.B.Cs. 3,350,000; W.B.Cs. 20,250. Under inhalation anesthesia, 11/1/41, products of pregnancy were removed; right salpingo-oophorectomy and supravaginal hysterectomy being performed by D. W. Goldman and W. F. Guerriero. Transfusions given. Postoperative course uneventful except for slight infection at upper part of incision. Discharged 11/14/41.

X. S. E. (I-41-28083), single, G. I., was admitted 6/17/41 complaining of generalized abdominal pain. LMP 10/17/40. History of being treated for gonorrhea and syphilis. Findings were such as to cause a diagnosis of acute polyhydramnios with a dead fetus. B.P. 136/80; T. 99.6; P. 110; R. 22. Transfusions given. X-ray revealed fetus apparently dead with a breech presentation (Fig. 7). Cervix was long and undilated. Hgb. 60%; W.B.Cs. 36,900; R.B.Cs. 2,700,000. On 7/4/41 the abdomen was opened and a macerated fetus and placenta were removed, and marsupialization performed by O. V. Prejean and J. E. Warren.

Transfusions and sulfonamides were given postoperatively. Temperature was of the spiking type for over 3 weeks after operation. Discharged 9/10/41 in good condition.

XI. T. R. (L-41-34307), married, primigravida, was admitted 7/22/41 complaining of pains in the abdomen. LMP in September 1940. History of being treated for syphilis. Fetal movements absent for 2 days. B.P. 160/90, T. 100.2; P. 96; R. 20. Abdomen enlarged to the size of a 6 months pregnancy. Firm mass evidently a myoma palpable in the cul-de-sac. Cervix uteri small, firm, and pushed under the symphysis pubis. X-ray films compatible with extra-uterine pregnancy with fetus in L.U.Q. On 7/23/40 under



FIG. 7. A.P. x-ray film in Case X showing breech presentation with overlapping of cranial bones

inhalation anesthesia a macerated female fetus was removed and a supravaginal hysterectomy, and bilateral salpingo-oophorectomy being performed by D. Goldman and R. E. Arnell. Uterine fibroids were present. Transfusions were given. Her maximum temperature was 103 on the second postoperative day. Patient afebrile after 3rd day and discharged 8/8/41.

XII. B. N. (L-41-42400), married, P. I, G. II, was admitted 9/6/41 complaining of pains in abdomen occurring every 15 minutes. LMP in January 1941. Findings were compatible with pregnancy at term with a fetus in transverse lie. B.P. 130/80; T. 101; P. 120; R. 30. Heart tones were clearly heard. The cervix was long and approximately 1 cm. dilated. The myoma was palpable in the cul-de-sac. X-ray films were strongly suggestive of an extra-uterine pregnancy. Hgb. 58%; R.B.Cs. 3,970,000; W.B.Cs. 12,650. Trans-

fusions were given. On 9/30/41 laparotomy was performed by W. F. Guerriero and Hughes. A living infant delivered; bilateral salpingo-oophorectomy, supracervical hysterectomy being performed. The uterus was 3 times its normal size and contained myomata. On the 8th postoperative day, patient had 7 convulsions and her B.P. reached 200/100. Cerebrospinal fluid proved to be clear. Afterwards she ran a febrile course due to pyelonephritis and required cystoscopy. She recovered.

XIII. F. W. (L-42-24106), married, primigravida, was admitted with a complaint of pain in the abdomen. LMP 3/14/41. History compatible with tubal rupture 9/15/41. B.P. 122/92; T. 98/6; P. 80; R. 20. Findings indicated the necessity for hystero-graphy; consequently, skiodan was injected into the uterus and the fetus proved to be ectopic (Fig. 8). Hgb. 92%; R.B.Cs. 4,400,000; W.B.Cs. 9,150. 3/7/42 the patient was laparotomized and the products of pregnancy removed. A right salpingo-oophorectomy and Norris hysteropexy being performed. The placenta was attached to the right tube and



FIG. 8. Hysterosalpingogram in Case XIII proves fetus to be extra-uterine

ovary and these were removed. B. J. Lehmann and W. F. Guerriero performed the operation. Patient's postoperative course was satisfactory and she was discharged on 9/17/42.

XIV. C. M. (L-42-63342), single, primigravida, was admitted 9/19/42 complaining of bleeding via vaginam and pain in R.L.Q. LMP in June, 1942. History compatible with tubal rupture in July. B.P. 110/85; T. 99; R. 95; P. 25. Tenderness and rigidity in the R.L.Q. Cervix firm and in normal position. Right adnexal mass extremely tender. 10/9/42 laparotomy performed by E. Bertucci and H. Cohen; the fetus removed from the abdominal cavity and right salpingo-oophorectomy being done. Hgb. 73%; R.B.Cs. 2,950,000, W.B.Cs. 5,250. Patient's subsequent course satisfactory. Transfusions given. She was discharged on 10/20/42.

XV. F. B. (T-43-110782), married, primigravida, was admitted 10/22/43 complaining of severe pain in the lower abdomen. LMP January, 1943. History compatible with tubal rupture in March. B.P. 180/110; T. 98.6; P. 80; R. 22. Fetal heart tones heard on admission. X-ray films revealed no overlapping of fetal bones; however, fetus appeared to

be in poor position. Diagnosis of toxemia of pregnancy made. Medical inductions were given. Admittance of a finger beyond the internal os disclosed no fetal parts or membranes. Fetal head was posterior to the fundus uteri. Diagnosis of abdominal pregnancy was made. Hgb. 70%; R.B.Cs. 3,650,000; W.B.Cs. 10,200. 11/26/43 under inhalation anaesthesia, the abdomen was opened and fetus removed. Supracervical hysterectomy and left salpingo-oophorectomy were performed by G. J. Mitchell and F. B. Hodnette. Patient's subsequent course uncomplicated. Discharged 12/10/43.

XVI. P. S. (L-43-115699) single, G. II, P. I, was admitted 1/18/44 complaining of severe pain in the left loin. History compatible with tubal rupture. B.P. 120/90; T. 100; P. 108; R. 40. Soft tissue technique x-ray films revealed abdominal pregnancy. Hgb. 80%; R.B.Cs. 3,470,000; W.B.Cs. 12,450. 1/19/45 under inhalation anaesthesia, abdomen opened, the fetus and placenta removed. Left salpingectomy, supracervical oophorectomy and the removal of a 7 months fetus performed by R. F. Phillips. The fetus appeared to be abnormal and lived only 2½ hours during which time it had 2 convulsions. Patient's post-operative course very stormy. Transfusions given. She was discharged 3/18/44 in good condition.

XVII. H. R. (T-44-137973), married, G. II, was admitted 5/26/44 complaining of sharp pains in the lower abdomen. LMP March 10, 1944. History compatible with ruptured tubal pregnancy in April. B.P. 110/74; T. 99; P. 94; R. 24. Generalized abdominal tenderness. Tympanitis present. Cervix soft and in an anterior position. Uterus enlarged to the size of an 8 weeks gravid state and displaced anteriorly by a cul-de-sac mass. Diagnosis of ruptured ectopic pregnancy made. Transfusions given. Hgb. 45%; R.B.Cs. 2,300,000. Under inhalation anaesthesia, 5/27/45, abdomen opened and a 4½ months fetus removed with membranes intact. A right salpingo-oophorectomy was performed, as the placenta was attached there. D. W. Beacham and G. J. Mitchell were the operators. For the first 5 days, patient's course was complicated by high fever, but she remained afebrile after that time. Discharged 8/25/44.

XVIII. M. W. (T-44-148558), married, P. I, G. II, was admitted 8/16/44 complaining of pain in abdomen. LMP in April. History compatible with tubal rupture. B.P. 122/65; T. 101; P. 130; R. 25. Abdomen distended and tympanitic. Cervix enlarged; bluish and soft. A mass in the cul-de-sac was palpable. Hgb. 2.5 gms; R.B.Cs. 1,270,000; W.B.Cs. 12,840. 8/17/44 under cyclopropane anaesthesia, the abdomen was opened and a living 4½ months fetus was removed from the abdominal cavity. The placenta was attached to the right tube; consequently a right salpingectomy and partial oophorectomy were performed and the operators were D. W. Beacham and C. G. Callender. Transfusions were given. Postoperative course quite satisfactory and discharged on the 9th postoperative day.

XIX. L. M. C. (T-44-161919), M.-S., G. II, was admitted 12/29/44 complaining of "knot in stomach." History compatible with tubal abortion. Cervix was pushed anteriorly behind the symphysis and a cystic mass was palpable in the cul-de-sac. B.P. 120/80; T. 101; P. 100; R. 22. Diagnosis of abdominal pregnancy was made and the patient operated upon 12/31/44. Procedure: supracervical hysterectomy; left salpingo-oophorectomy were performed by O. R. Depp and J. A. Holmes. Hgb. 62%; R.B.Cs. 4,100,200. Transfusions were given. Patient discharged 1/9/45.

XX. L. W. (L-42-39514), M.-S., G. IV, was admitted 9/15/44 complaining of pain in lower abdomen. History of having been treated for syphilis and pyonephritis. In 1942 Cesarean section had been performed because of cephalopelvic disproportion. History compatible with tubal rupture in May 1944. Findings compatible with extra-uterine pregnancy. Patient operated upon 9/16/44. The placenta was attached to the uterus and the pregnancy had undergone calcification. Uterine fibroids were present. Supracervical hysterectomy and bilateral salpingo-oophorectomy performed by J. M. Travis and D. W. Goldman. Patient was discharged 9/26/44 in good condition.

#### SUMMARY & CONCLUSIONS

1. The available literature concerning abdominal pregnancy or advanced ectopic gestation has been studied and the records of 20 cases managed at the

New Orleans Charity Hospital during the 8-year period ending June 30, 1945, have been reviewed.

2. Certain brief historical data have been presented.

3. The condition has been considered as to racial, age, gravidity, and general incidence. Character of previous pregnancies, if any, has been mentioned.

4. Etiology and pathology have been discussed.

5. The value of a carefully obtained history has been emphasized. Every attempt must be made to ascertain just what has transpired since conception occurred. Investigation in this Charity Hospital group resulted in classifying all of the cases as being secondary in type inasmuch as there was evidence of the occurrence of tubal abortion or tubal rupture in each case. Especial emphasis is placed upon the history of the "abnormal feeling" due to the location and movements of the fetus. Abdominal pain was a common chief complaint in the Charity Hospital series. Pseudo-labor is usually experienced by the cases that reach term. Symptoms due to fetal expiration are set forth.

6. The importance of a thorough physical examination is discussed. Early, pain upon movement of the cervix uteri and a palpable extra-uterine mass may be two of the most important findings. The significance of a high or transverse position of the fetus, abdominal tenderness, superficiality of fetal parts, easily palpable fetal movements, loud fetal heart tones, abnormal position of the uterine cervix, cervical softening with little or no dilatation and the absence of effacement, non-palpable round ligaments, and emptiness of the uterus are set forth.

7. Roentgenographic findings are discussed. Soft tissue technique x-ray films are of value in many instances, but in others hystero-graphy is required for accurate diagnosis.

8. Laparotomy should be performed as soon as the diagnosis is made unless the pregnancy is near term and the fetus is alive, in which event operation may usually be postponed until approximately the 36th week of gestation provided the general condition of the mother is good and she is kept under continuous hospital observation.

9. The decision as to removal of the placenta should be governed by the findings in each case. If its location is unfavorable and its blood supply is difficult to control, it should be left in the abdomen without drainage. In the presence of infection, chemotherapeutic agents are indicated.

10. Blood transfusions constitute an important part of the successful management of abdominal gestation cases.

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Although it would appear that the increased incidence of the dolichopellic type in these Negro women over the white group might be explained on the basis of racial influence, a study by Greulich and the author in 100 white women in a more privileged economic group than the present series of 500 white ward patients showed an even greater tendency toward dolichopellism than the Negro group.

Undoubtedly, numerous factors contribute to the variations of the adult female pelvis, among which those which are concerned with nutrition seem to be of prime importance. In a comparison of body build with pelvic type, Greulich, Thoms and Twaddle found a high incidence of dolichopellic and mesatipellic pelves among the largest women. They believed that such a finding "suggests the possibility that nutritive and other factors which make for the attainment of maximum normal growth tend to prevent that degree of anteroposterior flattening of the pelvis which has come to be regarded as characteristically feminine." Allen and Nicholson, more recently, have found that nutrition is an important factor in the ultimate shape of the pelvis. 2 figures.

## A TOXIC PRINCIPLE FROM PROGESTATIONAL ENDOMETRIUM AND PLACENTA

C. L. SCHNEIDER

Proc. Soc. Exper. Biol. & Med., 62: 322-325, 1946

Saline extracts of pregnant rabbit uteri and placenta have been shown to have toxic properties. The possibility that this toxicity might have some relation to toxemia of pregnancy has been expressed. In the present study extracts of different portions of the uterus in different functional states from several animal species, as well as extracts of liver, intestine and skeletal muscle, were studied by a method for quantitative estimation of the toxic effect. Young white mice were used for test animals.

After intravenous injection of toxic doses of active extracts the mice almost immediately became comatose and apneic. Some had convulsions; most either died immediately or rapidly recovered. In a few animals, clotted blood was found in the mesenteric veins and vena cava after death, but these could not be identified as ante-mortem clots and no other anatomical findings explained the deaths. In mice and rats, and apparently also in rabbits and dogs, an increase in tolerance could be built up by repeated injections of toxic extracts. Intramuscular, intraperitoneal and subcutaneous injections of 60 times the fatal intravenous dose failed to produce any significant response.

All of the highly toxic extracts were derived from preparations which contained endometrium or placenta. Extracts of skeletal muscle had a relatively mild toxic effect, but whether this effect represented the action of a substance identical to that found in the endometrium and placenta was not determined.

# PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

## A DISCUSSION OF PELVIC VARIATION AND A REPORT ON THE FINDINGS IN 100 NEGRO WOMEN

HERBERT THOMS

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The author presents the following classification for pelvic types:

1. *Dolichopellic Type*.—The anteroposterior diameter of the inlet is longer than the transverse.

2. *Mesatipellic Type*.—The anteroposterior and transverse diameters of the inlet are equal or the transverse diameter is no more than 1 cm. longer than the anteroposterior.

3. *Brachypellic Type*.—The transverse diameter is more than 1 cm. and less than 3 cm. longer than the anteroposterior diameter.

4. *Platypellic Type*.—The transverse diameter is 3 cm., or more, longer than the anteroposterior diameter.

The shape of the pelvic inlet in early childhood is characteristically elongated anteroposteriorly, or dolichopellic, and it would appear that the round or flattened forms of the adult female pelvic inlet may arise as a result of either an excessive growth laterally, or a diminished growth anteroposteriorly.

Evidence is presented which shows that the adult female pelvis in the white and black races is subject to considerable variation. Furthermore, while certain sex characteristics of male and female pelves can be accepted as more or less constant, others formerly thought to be constant are highly questionable. "Normal" variations in anteroposterior and transverse relationships are apparently present in both sexes in wide distribution.

A summary of the pelvic findings on 500 white primigravid women shows that 22.6 per cent were of the dolichopellic type, 46.6 per cent were of the mesatipellic type, 28.8 per cent were of the brachypellic type, and 2.0 per cent were of the platypellic type. Similar pelvic type distribution findings in the present study of 100 primigravid Negro women were: dolichopellic type, 29.0 per cent; mesatipellic type, 43.0 per cent; brachypellic type, 25.0 per cent; and platypellic type, 3.0 per cent.

In this series of 100 Negro women, no correlation between pelvic type and geographical distribution was noted. The clinical course of labor was reviewed, and the operative incidence for pelvic indications in the various groups was found to be as follows: dolichopellic, 6.8 per cent; mesatipellic, 4.6 per cent; brachypellic, 12.0 per cent; and platypellic, 66.6 per cent. Although this series is small, the evidence presented bears out findings previously seen in a much larger group of white women; that is, that the round (mesatipellic) or elongated (dolichopellic) pelvis is more favorable for natural birth than the oval (brachypellic) or the flat (platypellic) pelvis.

# MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

## DIETARY REQUIREMENTS IN HUMAN PREGNANCY AND LACTATION. A REVIEW OF RECENT WORK

R. C. GARRY AND HELEN O. WOOD

Nutrition Abstr. & Rev., 15: 591-621, 1946

In the 10 years which have elapsed since the authors' previous review on nutrition in pregnancy and lactation, surprisingly few fundamental additions have been made to the scientific knowledge of the subject. If anything, a more critical attitude has developed, and biologists are becoming humble in face of their great ignorance of the relationship between nutrition and pregnancy and lactation. One fundamental finding stands the test of time, that an ample diet of natural good foods is desirable both in pregnancy and lactation as in other periods of life.

However, our scientific knowledge is important, as it enables us to keep watch on undesirable practices in processing and in preparing foods for human consumption, and may help to direct into better channels the dietary habits of communities. Also, it enables the physician and obstetrician to take rational therapeutic steps to combat individual pathologic deviations from normal. But it is quite certain that reproduction is not in itself a pathological process and that, if pregnancy and lactation seem to require inevitably routine mass therapeutic measures, then we may assume that something is wrong with modern living, or in the interpretation of our information.

Standard tables of food allowances necessary for human beings at different periods of life are, at any given time, approximations and incomplete. Unfortunately, they are not infrequently regarded as permanent definitive standards. "Advertisers of vitamin products are almost universally guilty of this type of misuse of the table." (Wilder, 1945.)

During the war years the loss of infant life has decreased; nutrition is the only factor which improved during these years. It might be argued that this increase in reproductive efficiency was a result of earlier childbearing, but Baird found that the war made no appreciable difference in the age of women bearing children. On the other hand, the stillbirth- and neonatal death-rates have shown little improvement. Here the cause would appear to be factors operating in pregnancy. Prematurity, the commonest cause of neonatal death, is thought to be due largely to defective maternal diet. Recent social and dietary studies of different economic levels of the population have shown that the poorer sections have a poor diet on any "standard", and the reproductive efficiency of these sections, although they produce the majority of children in the nation, is inferior to that of women in better social circumstances. Inferior nutrition is not, of course, the only factor militating against successful reproduction when people

Endometrium under progesterone influence, as in the secretory phase of the menstrual cycle, pseudo-pregnancy or pregnancy, produced a more toxic extract than endometrium in other physiological states.

The toxic substance was not extractable in ether, acetone or alcohol. It was lost on heating to 75°C. for 10 minutes, addition of ethyl alcohol to a concentration of 25% or more, or upon acidifying the solution to pH 5. It did not dialyze through a cellophane membrane. Storage, even at low temperature, resulted in reduction of toxicity. Loss of toxicity of tissue extracts was considerably accelerated at room temperature by the addition of serum of mice or rats. Toxic extracts of skeletal muscle, placenta and endometrium were all inactivated by serum.

The properties of this toxic material, particularly its failure to dialyze, suggest that the substance is not histamine itself.

(For half a century and more, countless investigators have made countless extracts of the placenta and have maintained that they could produce convulsions in experimental animals with them and other changes suggestive of the toxemias of pregnancy. But, by and large, all these extracts have come to naught. Often as not, indeed, equally toxic extracts could be made from the liver, lung or other organs, which is tantamount to saying that these placental extracts lacked specificity. Hence, most of us have grown rather skeptical about studies such as the above and would want overwhelming evidence before believing that any given substance extracted was the cause of the toxemias.

Nevertheless, there is another side to this question. Despite the dearth of experimental evidence, the suspicion cannot help lurking in the minds of most obstetricians that some kind of a toxin must be produced by the placenta in the toxemias, elusive though it may be; and sooner or later a specific toxin may very possibly be found. Accordingly, it is well that efforts along these lines be continued, particularly when they are in the hands of such a competent investigator as Schneider. He brings to this problem an unusually rich background in biological research and is well acquainted with all the pitfalls involved. It is hoped, therefore, that just as soon as he gets out of the Army he will continue these promising investigations,—difficult though his objective may be.—Ed.)

tion and infancy are really understood, we may rely on foods naturally rich in vitamin D.

At present there is no satisfactory evidence that vitamin E plays any essential role in human reproduction

The prothrombin level of the infant's blood is, for some days after birth, lower than the accepted normal level for adults. It has still to be established, however, that the administration of vitamin K either to the mother shortly before birth or to the baby immediately after birth is justified.

If a natural diet is properly chosen, there should be no need for supplementation with B vitamins. In many parts of the world human diets seem to be on the borderline, and pregnancy creates a frank deficit. Supplements, when necessary, should be in the form of natural sources of the entire complex, since recent experiments by Richards on rats indicate that excess of a single member of the group, B<sub>1</sub>, may create a relative deficiency of another member, vitamin B<sub>6</sub>, pyridoxine.

The requirements for vitamin C in pregnancy, lactation and infancy are uncertain. Careful choice of diet, even in the absence of citrus fruits, probably provides a sufficiency of the vitamin for mother and child, although the levels recommended by many authorities cannot be attained in this way.

(The belief is growing on the part of competent observers that premature labor is due in large measure to defective maternal diet. Not only do Garry and Wood set forth this conviction in the above article but two other papers, abstracted in the present issue of the *SURVEY*, advance similar opinions (next abstract; and Tyson, Page 821). If this be true—and, as we shall see, there is considerable evidence that it *is* true—obstetricians as well as nutritionists face here one of the greatest opportunities in all medicine for the mass saving of human life.

It is common knowledge that prematurity is the principal cause of death in the neonatal period, accounting for about one-half of all fatalities occurring at that time. During the past decade pediatricians and public health officials, working chiefly in metropolitan centers, have made significant inroads on this toll, but they would be the first to affirm that the salvage, particularly in the smaller weight groups, is still discouragingly small. The country over, meanwhile, the death rate from prematurity shows little change from year to year. There are two main ways of attacking this problem. In the first place, mortality rates could be lowered substantially by wider dissemination of existing knowledge together with better distribution of personnel and facilities. This is a pediatric and public health responsibility. The other means by which premature mortality might conceivably be reduced is through the prevention of premature birth,—obviously a challenge to the obstetrician.

The question is, of course: could this challenge be met, more or less, by a wide-spread program emphasizing the necessity of better-balanced diets for all expectant mothers?

In the last few years several prenatal studies on large numbers of women have been carried out which have included evaluation of their diets during pregnancy. The first reports of this type to gain widespread attention were the Toronto studies of Ebbs, Tisdall and their associates. A group of 120 women on poor diets and low incomes were studied during the last half of pregnancy as controls for 90 women from the same income level and on equally poor diets but who were supplied with supplementary rations of milk, cheese, oranges, tomatoes, wheat germ and vitamin D capsules. Still a third group was followed comprising 170 women with fairly adequate incomes who were instructed in the type of diet considered desirable for pregnancy. The findings in relation to the question at hand were

are poor, but stillbirths, premature births and neonatal deaths, so long regarded as the hard core in loss of new lives, seem now to be yielding to improved nutrition of the mother.

The fear that ample nutrition in pregnancy may lead to excessive, and obstetrically undesirable, growth on the part of mother or fetus seems to be unwarranted.

Practically nothing has been added to our knowledge of the requirements for the proximate principles of diet. Some writers advise curtailment of carbohydrate intake during pregnancy; others do not favor such restriction. There is now little demand for very generous intakes of protein in pregnancy, and, at the same time, the fear of protein, when kidney function is impaired, is fast disappearing.

The metabolism of water and salt has been studied to find if fluid retention during pregnancy is a truly normal occurrence. Increase in blood volume, without corresponding increase in blood cells, seems to be physiological. Hemoglobin levels which do not fall below 80 per cent of the non-pregnant normal value are not pathological. Other extracellular fluids of the body seem also to share in this increase. This retention of water, however, may easily overstep normal limits, as in pre-eclampsia and eclampsia. Whether or not excessive salt "indulgence" is a causal factor, restriction of salt intake seems to be an effective therapeutic measure when pregnancy toxemia is feared.

Where there is reason to fear deficiency of iodine in the food, especially in regions where goitre is prevalent, it is desirable to give iodine in the form of iodised salt or cod liver oil throughout pregnancy and lactation.

There should be no lack of calcium, phosphorus or magnesium if ample supplies of milk and green vegetables are available for pregnant and nursing women. During lactation the calcium balance is negative for some little time, but the modern tendency is to lay little stress on this fact. If the woman is receiving a good ample diet, attempts to abolish such a negative calcium balance are looked upon with little favor, and supplementation of the mother's diet with simple calcium salts, with or without vitamin D, is deprecated. It is doubtful, too, if any attempt should be made to enhance the calcium retention of a baby at the breast by vitamin D administration.

The cause of anemia of pregnancy, after allowing for physiological hemodilution, should be sought in the diets of women before pregnancy.

By adult standards, infants at breast are "anemic" but the "anemia" occurs when the baby has iron stored in its liver and spleen. It has yet to be proved that iron administration in early infancy is of real benefit.

The idea that vitamin A is a specific anti-infective agent has lapsed. Yet, nobody seems to know quite why, a very large intake of this vitamin is recommended in pregnancy and lactation. Nevertheless, such an intake can be attained on a well-chosen natural diet. In some parts of the world infantile xerophthalmia, due to lack of vitamin A, is a real menace.

Fortification of foods with vitamin D was justifiable as a war emergency measure. But until calcium and phosphorus metabolism in pregnancy, lacta-

that "a rise in spending power led to an increased consumption of milk, fruit, vegetables and meat and a decreased consumption of bread and total cereals." (McCance, R. A., Widdowson, E. M., and C. M. Verdon-Roe: *A Study of English Diets by the Individual Method: III. Pregnant Women at Different Economic Levels*, *J. Hygiene*, 38, 596, 1938.) Taken alone the findings in the Johns Hopkins study cannot be accepted as establishing a relationship between dietary deficiencies and premature labor, but when taken in correlation with other types of evidence, the conclusion is inescapable that faulty nutrition deserves serious consideration as a possible cause of the dramatic differences in the incidence of prematurity which were encountered in this series.

All in all, then, the evidence is extremely suggestive that faulty nutrition in pregnancy may play an important role in the causation of premature labor. The practical implications of this statement are plain enough; and as said above, in all medicine there is no field which offers greater opportunities for the saving of human lives than does the prevention of premature birth.—Ed.)

## MATERNAL NUTRITION AND FETAL DEVELOPMENT

ANONYMOUS

Nutrition Rev., 4: 175-176, 1946

The effect of maternal nutrition on the general physical well-being of infants at birth and during the neonatal period has been studied by a group of investigators in the Department of Child Hygiene at the Harvard School of Public Health. A statistically significant relationship was demonstrated between the maternal diet and the infant's condition. Of the infants born to mothers whose diets were "excellent" or "good", 42 per cent were rated as "superior", 45 per cent as "good" and only one infant as "poorest." However, of infants born to mothers whose diets were "poor" to "very poor", only one was "superior" and one "good", while 67 per cent were rated as "poorest." In the 216 cases studied, all stillborn infants, all but one of those which died within the first few days of life, all premature infants, all of those "functionally immature" and a majority of those with marked congenital defects were born to mothers whose prenatal diets were very inadequate. A relationship was likewise noted between maternal diet and the course of pregnancy. Those mothers whose diets were "poor" or "very poor" had a tendency to pre-eclampsia, more difficult types of labor and more major complications at delivery than those whose diets were "good" or "excellent." Since the relationship between maternal diet and the course of pregnancy was less marked than that between maternal diet and the condition of the infant, the authors conclude that when the mother's nutrition is deficient, the fetus suffers to a greater extent than the mother.

Burke and Stuart have found that a significant relationship exists between the protein content of the mother's diet and the birth length and birth weight of the infants and their physical ratings. They concluded that when the maternal diets during the latter part of pregnancy contained less than 75 g. of protein, the infants tended to be short and light in weight and were most likely to receive a

most dramatic: the incidence of premature birth in the women with poor diets was 8.0 per cent; in those with supplemented diets 2.2 per cent; and in those with good diets 3.0 per cent. The corresponding figures for miscarriages were 6.0, 0.0 and 1.2 per cent; and for stillbirths, 3.4, 0.0 and 0.6 per cent. (Ebbs, J. H., Tisdall, F. F. and W. A. Scott: *The Influence of Prenatal Diet on the Mother and Child*, J. Nutrition, 22, 515, 1941; Ebbs, J. H., Scott, W. A., Tisdall, F. F., Moyle, W. J., and M. Bell: *Nutrition in Pregnancy*, Canad. M. A. J., 46, 1, 1942; Ebbs, J. H., Brown, A., Tisdall, F. F., Moyle, W. J., and M. Bell, *The Influence of Improved Prenatal Nutrition upon the Infant*, Canad. M. A. J., 46, 6, 1942; Ebbs, J. H.: *Nutritive Requirements in Pregnancy and Lactation*, J. A. M. A., 121, 339, 1943.)

Burke and her associates have likewise found that a statistically significant relationship exists between the diet of the mother during pregnancy and the condition of the infant at birth and during the first two weeks of life. The various phases of the extensive observations made by Burke and her group have been published in a series of articles one of which is abstracted below. In connection with the question under discussion it should be noted particularly that in the 216 cases studied, all stillborn infants, all infants who died within a few days of birth except one, most infants who had marked congenital defects, all premature and all functionally immature infants, were born to mothers whose diets during pregnancy were very inadequate. (Burke, Bertha S., Beal, V. A., Kirkwood, S. B., and H. C. Stuart: *The Influence of Nutrition during Pregnancy upon the Condition of the Infant at Birth*, J. Nutrition, 26, 569, 1943.)

A number of mass studies of the outcome of pregnancy in relation to diet have been made in England with similar findings. The People's League of Health of England investigated the effect of the nutrition of 5200 pregnant women upon maternal and infant morbidity and mortality. Supplementary minerals and vitamins were given to one-half of the women studied. The supplementary feeding tended to reduce the incidence of toxemia approximately 30 per cent while the reduction in the number of premature births in the supplemented group was also statistically significant. In another study made in England and Wales by Balfour, 11,618 pregnant women chosen from the lowest income groups were fed a supplement of marmite or other yeast extract sufficient to furnish 240 I.U. of thiamine daily, or a proprietary preparation which furnished a rich supply of vitamins A and D, as well as calcium, phosphorus and iron. Their controls were 8095 women from the same area. The supplementary feeding resulted in a statistically significant reduction in the number of stillbirths and in the neonatal mortality rate. (Interim Report of the People's League of Health: *Nutrition of Expectant and Lactating Mothers*, Lancet, 2, 10, 1942; Balfour, M. I.: *Supplementary Feeding in Pregnancy*, Lancet, 1, 208, 1944.)

In view of the above observations we have been particularly struck by a recent study made at the Johns Hopkins Hospital which seems to show a very definite relationship, in our clientele at least, between the incidence of prematurity and economic status. In an effort to inquire into the possible roles played by economic and racial factors in the initiation of premature labor, 24,321 cases of labor in which the pregnancies were single and the onset of labor spontaneous, were divided into three groups: private patients, white ward patients and colored ward patients. The incidence of premature labor in private patients was 5.3 per cent; in white ward patients, 7.6 per cent; and in colored ward patients, 13.4 per cent. In other words, as one went down the economic scale the frequency of premature labor augmented sharply, the incidence in white ward patients being 50 per cent higher than in private patients, and in colored patients, two and a half times as high. Moreover, this relationship held true at all weight levels. Thus, for infants weighing between 2000 and 2499 grams, the corresponding figures were: 3.8, 4.9 and 8.9; for infants weighing between 1500 and 1999 grams, they were: 1.0, 1.8 and 3.1; and for infants weighing between 1000 and 1499, they were 0.5, 0.8 and 1.4. Although every effort has been made to ferret out some explanation for these figures other than economic status, we have been unable to do so.

As shown by McCance and his associates, economic level exerts an important influence on the intake of essential food elements such as minerals, vitamins and proteins; and in a study of the diets of a large number of pregnant women at various economic levels he found

impossible, sternal puncture may be of value. The author has given whole blood, plasma and glucose many times by this method, and is satisfied that the procedure has saved lives.

There can be no doubt that the general dietary trend in the past 10 years among students in nutrition has been towards an increase in protein intake. In pregnancy, edema is usually the first evidence of an advancing toxemia. Therefore, it is reasonable to deduce that any therapy, dietary or otherwise, which tends to reduce water retention should be desirable. The author advocates a high protein diet because he believes, as a result of his experience, that it very decidedly lessens the incidence of toxemia. A diet is presented which is high in protein and carbohydrate, and medium low in fat. Excessive salt is avoided. Skim milk powder (spray) is advocated as a sane and cheap method of supplying protein and calcium to those patients who do not tolerate fluid milk.

## ADEQUACY OF THE DIET DURING LACTATION

MILDRED KAUCHER, ELSIE Z. MOYER, H. H. WILLIAMS AND I. G. MACY

J. Am. Dietet. A., 22: 594-601, 1946

In an investigation of the secretion and composition of human milk, the authors have analyzed the foods eaten and the milk secreted by 12 multiparae during 31 five-day periods at various intervals postpartum. The mothers were successfully nursing their infants, were healthy throughout the investigation, and the babies grew and developed satisfactorily while receiving their mothers' milk. The diets were comparable qualitatively, but quantities were determined by the appetites of the women. By analysis the diets provided averages per day of 2928 calories, 109 gm. of protein, 129 gm. of fat, 1.2 mg. of thiamin, 3.1 mg. of riboflavin, 16 mg. of niacin, 7.9 mg. of pantothenic acid, 57 mcg. of biotin, and 33 mg. of vitamin A (including carotene).

The data obtained by analysis of the voluntary diets were compared with values calculated from the literature and with the allowances recommended for lactating women by the Food and Nutrition Board of the National Research Council, adjusted to the body weights of the women. The daily averages for all periods of study compared well with both the calculated values and the recommended allowances for energy, protein, riboflavin, niacin and pantothenic acid. Although the values obtained for thiamin and vitamin A by analysis were comparable with those calculated, they did not conform with the recommended allowances of the National Research Council. The thiamin intakes were about one-half, but the vitamin A intakes were  $1\frac{1}{2}$  times the recommendations.

In addition, the "net intakes" (amounts in food minus amounts secreted in milk) were compared with the recommended allowances for nonlactating women, adjusted to the body weights of the women. The adjusted recommended al-

low pediatric rating. Further analyses of the data have been presented by Stuart. It appears that the osseous development of an infant at birth depends to a considerable extent on the maternal diet. Among the infants born to mothers whose diets were "poor" or "very poor", only one was considered to have "advanced" osseous development while 63.9 per cent were "retarded." Among the infants born to mothers whose diets were "excellent" or "good", 27.6 per cent were rated as "advanced" and 10.4 per cent as "retarded." The relationship between the osseous development of the child and the protein content of the maternal diet was more striking than the correlation with the calcium level.

Stuart further analyzed the relationship between these findings and the health of the mother, particularly in regard to pre-eclampsia, nausea, vomiting and anemia. There were 28 cases of pre-eclampsia in the fair and poor to very poor diet group. Of the 28 infants born to these women, 23 failed to obtain a good rating. Of 16 cases with severe nausea and vomiting, 5 in the poor diet group and one in the fair diet group later had pre-eclampsia. The other 10 cases were rather evenly distributed between the various diet groups, and the infant's condition appeared to depend on the quality of the diet the mother succeeded in taking rather than on the nausea and vomiting *per se*. Of 11 cases of severe anemia, one mother had a "good to excellent" diet, 6 had "fair" and 4 had "poor to very poor" diets. Five of the 11 infants showed unsatisfactory physical condition at birth.

## SOME OBSERVATIONS ON THE ROLE OF PROTEIN IN PREGNANCY

E. M. BLAIR

West. J. Surg., 54: 288-293, 1946

The author discusses protein therapy from 2 standpoints: (1) obstetrical shock, and (2) obstetrical diet. Protein is the greatest single agent in combating shock in medical armamentarium. In shock, an initial vasodilatation causes circulatory collapse, with the result that intravascular fluid pours out into the extravascular spaces. Protein molecules, when added to the intravascular fluid or plasma, must, in great part, remain there because they are far too large to pass through the membrane into the extravascular fluid. As a result, concentration within the circulation is increased, osmotic pressure is increased and fluid is drawn from the extravascular spaces back into the circulation. In addition to this factor, one must consider the life of the individual cell. Osmosis may be considered the breath of the living cell, made possible by the presence of protein within the cell. Since shock interferes with cell osmosis, its only antidote is immediate and sufficient supply of water and protein. It is generally accepted that by far the best means of supplying protein to the patient in shock is by administering human whole blood and human plasma, preferably by intravenous therapy. In cases of profound shock, when intravenous therapy is difficult or

lateral bore, and malposition, indicating that a forceps operation may be unduly difficult.

It is felt that the present method of determining midpelvic volume by means of the interspinous diameter is inadequate, and much greater emphasis is placed on such factors as lateral bore, side walls, subpubic angle and sacrosciatic notch.

It is concluded that cephalometry and fetometry are too inaccurate to be of much importance in pelvioradiography.

Pelvic architecture played an important part in influencing the prognosis in the present series of cases. The prognosis became progressively worse in the following order: gynecoid, anthropoid, platypelloid and android. In the absence of disproportion, a favorable prognosis was usually given in the anthropoid and gynecoid types. The fetal-pelvic ratio was arbitrarily decided by the use of the precision stereoscope, and not by volumetric comparisons which were too often misleading.

Malposition influenced the prognosis unfavorably. The prognosis in breech presentation is based almost entirely on the pelvic measurements and architecture, and no trial of labor is advised in this presentation. In no case in this series where a vaginal delivery of breech presentation was advised did such a delivery terminate with fetal mortality.

The radiologic prognosis in these 500 cases was given on the basis of pelvimetry, pelvic architecture, fetal-pelvic relationships and presentation. A correct prognosis was given in 97.8 per cent of the series. In only 35 per cent of the cases in which dystocia was feared was operative delivery necessary. Sixty-five per cent were given a good prognosis, illustrating the conservative influence of pelvioradiography.

The limitations of pelvioradiography are assigned to the difficulty in estimating the soft tissue factors, behavior of the cervix, character of the labor contractions, the skill of the obstetrician, and the age and previous history of the patient.

(From time to time expressions of skepticism are voiced concerning the value of X-ray pelvimetry. It is alleged that roentgen pelvimetry has led to many unnecessary cesarean sections and, contrariwise, that it has often failed to demonstrate degrees of disproportion which were severe enough to cause subsequent dystocia. It is also claimed that the character of the uterine contractions, the condition of the cervix, and many others factor involved in parturition are so important that reliance on X-ray pelvimetry may be very misleading in regard to the outcome of any given labor.

It is hoped that the above article, together with others in the same vein, may help correct these unjust charges. But if X-ray pelvimetry is such a valuable agent in the hands of Weinberg and Scadron, what is the basis for the skepticism one hears expressed now and then? It seems likely that it may be due to neglect of one or more of the following considerations:

1. The films must be taken with meticulous precision by one of the techniques designed for pelvic mensuration. This would seem self-evident, but it is surprising how many patients give a history of "cephalo-pelvic disproportion on X-ray evidence" in their previous labor but who on careful roentgenographic mensuration show a huge pelvis and subsequently, and with ease, give birth vaginally to a child much larger than the previous one. Some of these patients bring their films along; often there is no evidence that a marker was used and not infrequently just a flat plate has been taken. Evidently some practitioners of obstetrics think they can get an impression of pelvic size from a flat plate just as they

allowances were: 2516 calories, 65 gm. of protein, 1.3 mg. of thiamin, 1.7 mg. of riboflavin, 12 mg. of niacin, and 1.2 mg. of vitamin A. The "net intakes" were, respectively, 2374 calories, 98 mg. protein, 1.1 mg. thiamin, 2.8 mg. riboflavin, 15 mg. niacin and 2.7 mg. vitamin A. The average "net intakes" during the puerperium were lower than those for periods of mature milk production, owing to the greater average milk volume produced during the first 10 days postpartum, and to the reduced activity.

The data presented in this paper are further evidence of the adequacy of the allowances recommended for lactating women. They demonstrate that some individuals maintain health on far less than the recommended amounts of nutriment; others require more. The results show that the recommended allowances for lactating women should not be used for feeding individual women or groups whose average weight is considerably over or under the 56 kg. used by the Food and Nutrition Board.

## THE VALUE AND LIMITATIONS OF PELVIOGRAPHY IN THE MANAGEMENT OF DYSTOCIA, WITH SPECIAL REFERENCE TO MIDPELVIC CAPACITY

A. WEINBERG AND S. J. SCADRON

*Am. J. Obst. & Gynec.*, 52: 255-263, 1946

The material upon which this study is based consists of 500 consecutive cases referred to the x-ray department because of dystocia, either actual or feared. These cases were studied with particular reference to the evaluation of midpelvic contraction in dystocia.

A comparison was made of techniques of roentgen pelvimetry by measuring the same patients by various methods. The pelvic diameters obtained by the precision stereoscopic method, the Thoms-Torpin isometric scale, and the Snow ruler and Ball nomogram gave results that in all cases differed no more than within 0.1 cm. from each other. It is concluded that, provided a reliable technique of roentgen pelvimetry is used, there is very little difference in the roentgen mensuration.

The authors consider that the sum of the anteroposterior and transverse diameters at any given pelvic plane is a more reliable index than the separate consideration of each, because they mutually compensate for each other. A statistical review of the pelvic measurements as obtained by the writers' method of radiopelvimetry in correlation with the ultimate mode of delivery reveals that if the inlet measurements are below 23 cm. and/or outlet measurements below 14 cm., dystocia is expected. For inlet dystocia the prognosis is guarded or poor, with a section to be considered. For outlet dystocia the prognosis is usually a forceps operation. The authors do not recommend section for outlet dystocia alone unless it is combined with other unfavorable factors such as android pelvis, narrow outlet, prominent spines, converging side walls and

(2) *Supero-inferior*, patient sitting inclined backwards, plane of inlet parallel to film, centering 2 in. behind symphysis, cone covering circle 10 in. diameter.

(3) *Lateral*, patient erect, centering 2 in. above upper margin of greater trochanter, cone covering circle 14 in. diameter.

(4) *Subpubic arch projection*, patient sitting inclined forwards, centering approximately over spinous process of third lumbar vertebra, cone as in (2).

The focus-film distance used in projections 1, 2 and 3 was 37 in., and in projection 4 it was 30 in.

In order to measure the doses received in the depths of the pelvis during pelvimetric examination, "thimble" ionization chambers were used. These were charged to a potential of 165 volts, enabling doses up to about 1.3 röntgens to be measured. The ionization chambers were placed in the posterior-superior limits of the vaginal vault. In relation to the bony walls of the pelvis, the chamber in each patient was 1.5 in. anterior to the sacro-coccygeal junction and

TABLE I

PATIENT	MATURITY	PROJECTION	kV	mA	TIME	F-F DISTANCE	RADIATION MEASUREMENT
						in.	r
A	14 weeks	1	70	40	2.5	37	0.39
		4	82	40	3.5	30	
		2	92	40	8.0	37	0.47
		3	92	40	5.0	37	
B	37 weeks	1	77	40	2.5	37	0.80
		4	85	40	3.5	30	
		2	100	40	8.0	37	
		3	88	40	6.0	37	

approximately 1.0 to 1.5 in. below and behind the mid-point of the true pelvic cavity.

The various physical and technical factors, and the results of the measurements, are presented in Table I. It is somewhat gratifying to note that even with this somewhat extensive pelvimetric examination (admittedly without the duplicated exposures of a stereoscopic technique) the dose received at the vaginal vault was less than 0.9 röntgen both early and late in pregnancy.

## THE RELIEF OF PAIN IN LABOUR WITH DEMEROL

W. D. FLATT

Canad. M. A. J., 55: 43-46, 1946

Demerol was used almost routinely for the relief of pain during labor on public ward patients at the Toronto General Hospital from February, 1945, to June, 1945. It was given to more than 200 patients, for the most part intramuscularly.

used to think they could gain such an impression by inserting two fingers in the vagina and palpating around about. Actually, nothing can be more misleading in regard to pelvic and fetal size than a flat plate. I remember a breech case in which the attendant had all plans made to perforate the after-coming head because a flat plate had shown an "enormous hydrocephalic" head. Repetition of the X-ray by one of the standard methods of mensuration revealed a head of normal size and this was confirmed at birth.

2. The films must be interpreted by one versed in the discipline. This cannot be learned overnight, but must be acquired through study and experience. The general pelvic architecture must be evaluated; the transverse diameters must be nicely correlated with the antero-posterior; the sharpness of the fore-segment must be considered; and the divergence or convergence of the lateral bore, the exact distance between the ischial spines, the available space beneath them, and many other factors must be weighed before assessing the potentialities of a given pelvis. X-ray pelvimetry has brought to obstetrics a new body of knowledge,—one that should be included in every program of house-staff training and one which is indispensable to establishing correctly the role which the pelvis will play in labor.

3. The films must be interpreted by an obstetrician. Here and there in the country are a few roentgenologists who have become especially interested in X-ray pelvimetry and have made, in some instances, notable contributions to the subject. They must be regarded as exceptions to the above statement. Their number, however, is negligible and in 99 cases out of 100, the opinion of a roentgenologist about a pelvimetry film is not dependable. Actually the evaluation of such a film requires a very exact and extensive knowledge of the mechanism of labor and of other factors which only an obstetrician can possess.

4. The X-ray findings must be correlated with the clinical. X-ray pelvimetry will rarely give a cook-book answer to a problem of dystocia and can never serve as a substitute for sound obstetrical judgment. Among the several factors involved in labor, however, the pelvis does loom large; and concerning this it will give precise information. The other factors concerned—the character of the uterine contractions, the condition of the cervix, the age and parity of the patient, the history of previous labors, etc.—must now be weighed in the balance against the pelvic picture. Because of these soft-part factors, X-ray pelvimetry cannot be expected to eliminate trial labors but it should reduce their frequency.

Weinberg and Scadron have shown very clearly what excellent prognostic results may be achieved with X-ray pelvimetry provided the above conditions are met. Our results have been similar but perhaps not quite so good.—Ed.)

## A NOTE ON THE AMOUNT OF RADIATION INCIDENT IN THE DEPTHS OF THE PELVIS DURING RADIOLOGICAL PELVIMETRY

J. H. MARTIN AND E. R. WILLIAMS

Brit. J. Radiol., 19: 297-298, 1946

Since among radiologists there has always been some unease in carrying out major radiological investigations during pregnancy, it seemed desirable to the authors to measure the amount of radiation incident in the depths of the pelvis during the performance of radiological pelvimetry. Two patients of similar general build were selected for investigation, one being 14 weeks pregnant and the other 37 weeks pregnant. On each patient, a full standard pelvimetric technique was carried out, appropriate to the stage of pregnancy. Briefly, the technique was as follows:

(1) *Antero-posterior*, patient supine, centering in mid-line 2 in. above symphysis pubis, cone covering circle of 17 in. diameter at 37 in.

## PATHOLOGY OF PREGNANCY

### A FIFTEEN-YEAR STUDY OF PREMATUREITY; FROM THE STAND- POINT OF INCIDENCE, MORTALITY AND SURVIVAL

RALPH M. TYSON

J. Pediat., 28: 648-664, 1946

This paper consists of a clinical and statistical survey of premature infants born at the Philadelphia Lying-In Hospital during the 15-year period beginning Jan. 1, 1930, and ending Dec. 31, 1944.

The average incidence of prematurity for the entire period was 9.4 per cent, with the highest incidence of 10.2 occurring in 1930, and the lowest of 7.5 in 1933. Fifty-nine per cent of the cases of prematurity occurred in mothers between 20 and 30 years of age. From 1937 on, there was a decrease in mothers under 20 and an increase in those over 30 who were delivered. Apparently, age of the mother, race and economic status did not influence the course of events. However, there is some reason to believe that competent prenatal care together with the faithful cooperation of the pregnant patient produced a favorable response. In 1932 a program of dietary control was initiated and, while this had no obvious effect on the number of premature infants, it apparently had a definite influence on the occurrence of increasing numbers of big premature infants (over 4 pounds) and of decreasing numbers of preivable babies under 2½ pounds (1000 gm.).

Of the 2960 premature infants born in this period, 1140 (38.5 per cent) died. The highest premature infant mortality (56 per cent) occurred in 1931, and the lowest (26 per cent) in 1940 and 1941. The birth weight of premature infants was undoubtedly an important factor in their survival. It appeared that premature babies born to mothers over 30 years of age are less viable than premature babies born to mothers of younger age. Infants, premature as a result of multiple birth, have a lower mortality percentage than single premature infants. Systemic diseases in the mother, especially toxemia, and complications of delivery including cord and placental complications, were extremely important in respect to the mortality rate. The methods employed in delivering these babies, with the exception of a breech presentation, assumed a less impressive position. Breech delivery is the most hazardous of ordeals for the premature infant.

The survival of the premature infant seems to be primarily dependent upon its birth weight, the absence of severe complications before and during delivery, and upon skillful care during the first few weeks of life. Important aspects of this care are the cautious administration of food, the avoidance of dehydration and infection, and the maintenance of a favorable environment. The ultimate prognosis of premature infants can be determined only by time because of the

It was not given to patients with eclampsia or severe pre-eclampsia; patients with mild pre-eclampsia suffered no ill effects from the drug. Intravenous injection of demerol resulted in immediate pain relief and intramuscular injection was followed by relief in from 5 to 15 minutes. The duration of drug action in both instances was from one to 3 hours. It was given alone, in combination with hyoscine, or in combination with hyoscine and sodium amytal.

The resultant effects on 200 mothers were as follows: complete amnesia and complete analgesia, 7.5 per cent; almost complete amnesia and complete analgesia, 9.0 per cent; almost complete amnesia and almost complete analgesia, 37.0 per cent; incomplete amnesia and almost complete analgesia, 21.0 per cent; incomplete amnesia and incomplete analgesia, 15.0 per cent; and no amnesia and no analgesia, 1.5 per cent. There were 9 stillbirths in this series, and the causes of death were as follows: pre-eclampsia, 2; syphilis, 1; premature separation of the placenta, 3; prolapsed cord, 1; anencephaly, 1; and hydrops fetalis, 1. No intrapartum fetal deaths were attributed to the sedation used. Almost immediate respiration took place in 73.4 per cent of the infants, delayed respiration in 21.8 per cent and prolonged resuscitation in 4.6 per cent. In no instance was prolonged resuscitation directly attributed to demerol. The sedation routine may have had some effect on the infant, since delayed respirations occurred most commonly cases where the mothers had had complete amnesia and analgesia, or almost complete amnesia and complete analgesia.

The most satisfactory method of sedation in the present series was as follows: demerol 100 mg., hyoscine gr.  $\frac{1}{150}$  with or without sodium amytal gr. 3; repeat demerol 100 mg. in one hour, then give demerol 100 mg. and hyoscine gr.  $\frac{1}{150}$  every 3 hours or when necessary. In general, the greatest success in providing satisfactory pain relief depends upon the brief interval between the first and second intramuscular injections.

Demerol is a synthetic coal tar product with atropine, morphine and papaverine-like properties which gives satisfactory relief from pain during the first and second stages of labor. It is safe, and can be given frequently. It produces excellent analgesia and sedation, and has a profound antispasmodic effect. Labor is not retarded and infant anoxemia is reduced to a minimum. It can be given more frequently than heroin and can be given quite safely at any time during the first or second stage of labor. It is of value during delivery where a general anesthetic is contraindicated or not available.

nosis of tubal pregnancy. However, a negative test does not rule out the possibility of old ruptured ectopic pregnancy. Peritoneoscopy may aid in the differential diagnosis of a difficult case. Colpotomy has been a valuable diagnostic procedure.

A correct preoperative diagnosis was made in 79.4 per cent of the patients, and pelvic inflammatory disease accounted for 35.5 per cent of the mistaken diagnoses.

Supplementary surgery in the management of ectopic pregnancy is not without hazard. The gross mortality rate was 2.6 per cent; the operative mortality was 2 per cent. The author believes that immediate operation and timely plasma transfusions, together with the judicious use of chemotherapeutic and antibiotic agents, will go a long way toward decreasing still further this low mortality rate.

### PREGNANCY IN HYPERTENSIVE DISEASE FOLLOWED BY THORACOLUMBAR SYMPATHECTOMY WITH RENAL BIOPSY AND COMPLETE RECOVERY

S. M. BOLTUCH

New York State J. Med., 46: 1362-1364, 1946

The present case is of interest for its uniqueness, the author having been able to find only one case of a pregnancy complicating hypertensive disease with renal biopsy findings.

The patient was a 32 year old white primigravida whose expected date of confinement was February 10, 1944. Except for a dilatation and curettage and excision of cervical polyps for menometrorrhagia in 1941, the past history was negative. The first trimester of pregnancy was uneventful; the blood pressure was 130/95. Urinalysis was negative for albumin and glucose, blood urea clearances indicated normal function, and complete cystoscopic examination showed no evidence of urinary tract abnormality. The pregnancy progressed uneventfully except for the persistence of hypertension, ranging between 140/85 and 150/95. In the 28th week of pregnancy albuminuria was first noted. This increased from slight to marked degree and by December 15, many hyaline and granular casts appeared. The blood pressure rose to 175/120. Funduscopy examination showed no neuroretinitis. The veins were full, but there was no arteriovenous nicking. The patient was hospitalized on December 16, and in spite of strict diet, complete bed rest and restricted fluid intake, her hospital course was characterized by gradually increasing blood pressure, to 235/155. On December 26 albuminuria continued, hyaline and granular casts occurred in increasing numbers and the patient complained of almost constant pain in the

possibility of the later appearance of abnormalities that were not evident during the early days of life.

(See editorial note on Page 811.)

## A TEN-YEAR SURVEY OF ECTOPIC PREGNANCY

R. C. NUCCI

Pennsylvania M. J., 49: 953-963, 1946

The author presents a statistical analysis of 150 consecutive cases of ectopic pregnancy. The incidence, on the basis of gynecologic admissions, was 1.46 per cent; on the basis of gynecologic laparotomies it was 2.91 per cent. The incidence was not found to be higher in the colored race.

Approximately 75 per cent of the cases occurred in patients between the ages of 21 and 35 years. Forty-four patients (29.3 per cent) had not previously been pregnant. Fifteen patients (10 per cent) had not been able to continue previous pregnancies to term. Twenty-four patients (16 per cent) gave a history of temporary sterility. Ten patients (6.6 per cent) had had previous ectopic pregnancies.

Thirty per cent of the series showed gross evidence of inflammation in the unaffected tube. Previous abdominal operations had been performed in 25.8 per cent of the patients. The author's observations emphasize the role played by inflammatory disease, previous abortions and postoperative adhesions in the etiology of ectopic pregnancy. In 4 cases ectopic endometrial tissue might have had some etiologic significance.

Pain and bleeding were the 2 commonest symptoms, occurring in 92 and 96 per cent of the cases, respectively. The diagnostic triad of pain, bleeding and missed or atypical period was present in 70 per cent of the series.

Blood studies, including sedimentation rates, were essentially normal in intact tubal pregnancies, with variations found to be due to concomitant pelvic inflammatory disease. In ruptured tubal pregnancies and tubal abortions lower hemoglobin readings and red blood cell counts prevailed; fluctuation in leukocyte counts was frequently observed and was influenced by the amount of hemorrhage and degree of concomitant pelvic infection. The sedimentation rate was of aid in differentiating intact tubal gestation from acute pelvic inflammatory disease.

A pelvic mass was noted in 62.5 per cent of the patients and adnexal tenderness in 65.7 per cent. Severe discomfort incident to movement of the cervix existed in 24 per cent. Curettage was of diagnostic significance in only 25 per cent of the 49 patients on whom it was performed. "Pregnancy glands" have the same diagnostic significance as decidual tissue. The biologic test, when evaluated in the light of clinical history and pelvic findings, can aid materially in the diag-

SPONTANEOUS RUPTURE OF THE LIVER IN ECLAMPSIA WITH  
FATAL HEMOPERITONEUM

S. SANES AND C. A. KAMINSKI

Am. J. Obst. &amp; Gynec., 52: 325-329, 1946

The authors present the clinical and postmortem findings in an eclamptic patient with spontaneous rupture of the liver and massive hemorrhage into the peritoneal cavity following induced labor and delivery.

The patient, a 26 year old Negro multipara whose expected date of confinement was some time in February, 1945, was admitted to the hospital on December 25, 1944, with convulsions. Other complaints included blurring of vision with spots before the eyes and ankle edema. The patient was well-developed and obese and the blood pressure was 200/145. No fetal heart sounds were heard. There was dullness in both flanks. The ankles showed 4 plus edema. No presenting parts could be palpated on rectal examination, and the cervix was not dilated. The urines showed a specific gravity of 1025 and 4 plus albumin.

During her first hospital day the patient continued to have convulsions and emesis, and treatment for eclampsia was instituted. On December 26 a sterile bougie was inserted through the cervix and the vagina was packed with sterile gauze. The membranes ruptured during the procedure. Subsequently, the patient was given pitocin and convulsions and emesis stopped; the blood pressure was 205/130. On December 27, the patient had one strong sustained contraction and precipitated the vaginal pack, bougie and a female infant weighing 2 pounds, 2 ounces. The secundines were expressed completely with the baby. Following the precipitate delivery the patient appeared drowsy, diarrhea developed and the pulse rate and temperature rose. The uterine fundus was firm. Four hours after delivery the patient rapidly became pale and dyspneic, abdominal distention developed and the blood pressure was 80/70. She responded briefly to treatment for shock, but soon expired. The clinical impression was "rapid internal hemorrhage."

The pathological diagnosis included the following findings: eclampsia, eclamptic lesions of the liver, subcapsular hemorrhage of anterior and posterior surfaces of both hepatic lobes, rupture of capsule of superior surface of left lobe of liver, massive hemoperitoneum with blood clots over left lobe of liver and hemorrhage of right rectus muscle.

The authors state that, while it is reasonable to assume that the eclamptic lesions of the liver could be the sole cause for the subcapsular hemorrhage and capsular rupture, other factors, including convulsions, vomiting and parturition, must be considered. Up to, and after the time convulsions and emesis stopped, the patient complained of no abdominal pain. The blood pressure remained high. It was following delivery, with a strong sustained contraction, that the patient became drowsy, pulse and temperature rose and diarrhea developed.

head. On January 3 she experienced sudden cramp-like uterine pains and vaginal bleeding. The blood pressure was 230/150, pulse 120, and fetal heart sounds were still present. The impression was partial separation of the placenta, and a low-flap cesarean section was performed. The placenta was three-fourths separated, one edge being attached to the anterior wall of the lower segment. A living, 3-pound, 12-ounce infant was extracted.

After an immediate drop in blood pressure, the former levels of 180/100 to 200/120 soon returned and were maintained until the patient's discharge from the hospital. Complete relief from headaches and complete disappearance of ankle edema occurred within 48 hours. Albuminuria gradually diminished to only a trace.

Two months postpartum the left retina was found to have a definite exudate below the macula, as well as greater nicking of the veins and occlusion in a few of the vessels. The patient had intermittent headaches, her blood pressure was 200/120, and albuminuria and occasional hyaline casts persisted. In spite of treatment during the next 3 months, the blood pressure remained between 200/100 and 230/120 with persistent 4 plus albuminuria, hyaline casts, severe headaches and nausea. On May 29, 1944, a right thoracolumbar sympathectomy was performed, and on June 6, the procedure was repeated on the left side. During the operation renal biopsy was performed. Pathologic examination revealed marked sclerosis of small arteries and arterioles with partial obliteration of lumina and sclerosis of glomeruli of various degree, and extensive round cell infiltration of the interstitial tissue. The patient recovered uneventfully, and during the next 18 months showed blood pressure levels of 110/80 to 115/85. No albuminuria or casts were present in the urine, eyeground examination was essentially negative and headaches disappeared.

The author concludes that the pregnancy in this case was the causative factor in producing the renal vascular lesion which, once established, aggravated the existing hypertension and did not subside after the pregnancy terminated. The sympathectomy gave relief, if only temporarily. It may be assumed from observations by Smithwick and Castleman that the renal damage after sympathectomies does not progress rapidly. For this effect alone, sympathectomies in young women postpartum are well worthwhile.

It is important, but often very difficult, to distinguish between chronic glomerulonephritis and pre-eclamptic toxemia. Until now, it was accepted that clinical conclusive evidence of chronic glomerulonephritis is the eyeground findings of albuminuric retinitis. In this patient the ocular findings were of the essential hypertensive type and, as proved by the renal biopsy, associated with arteriosclerosis of arteries and arterioles with early renal parenchymal involvement. One of the distressing features, for the obstetrician, of this type of disease is the likelihood of intrauterine fetal death or a premature separation of the placenta with no warning. In addition to the immediate dangers, these patients are usually left with permanent renal impairment by pregnancy. 2 figures.

## HYDATIDIFORM MOLE, WITH SPECIAL REFERENCE TO RECURRENCE AND ASSOCIATED ECLAMPSIA

L. C. CHESLEY, S. A. COSGROVE AND J. PREECE

Am. J. Obst. &amp; Gynec., 52: 311-320, 1946

The case is presented of a patient who had a hydatidiform mole in her first pregnancy. This mole was accompanied by severe pre-eclampsia. Three months following the extrusion of the mole, the Friedman test became repeatedly positive, after having been negative. No reason ever was found for this. The patient then had 3 pregnancies without mole and without toxemia. Two of these were characterized by anomalous placentation. Her fifth pregnancy was again molar, and with this mole she had eclampsia. Five weeks after the mole was expelled she developed signs of chorionepithelioma, and this diagnosis was confirmed. The Friedman test was negative at 3 weeks and only weakly positive at 5 weeks, despite the presence of the neoplasm. Cystic ovaries occurred with both of the moles.

In a review of the literature the authors have found about 40 cases of recurrent hydatidiform mole. Only 5 of these women had normal pregnancies between moles. The authors have found 35 cases of probable or alleged eclampsia in conjunction with hydatidiform mole. In the 36 cases, including that reported in this paper, there was a mortality rate of 14 per cent. This seems low when one considers the mortality rate for mole alone, or for eclampsia alone, during the times when most of these cases occurred. The ratio of primiparas to multiparas is 2 to 3, which is at distinct variance with the ratio of 3 to 1 in any considerable series of eclamptic patients.

In over 75,000 deliveries at The Margaret Hague Maternity Hospital, there have been 57 cases of hydatidiform mole (through 1944), or an incidence of one in 1321. Cystic ovaries were diagnosed in 4 of these cases. A fetus was present in 4 cases. There were no maternal deaths. Among the signs and symptoms, bleeding occurred in 96.6 per cent. Secondary anemia was observed in 19 patients. The uterus was larger than to be expected from the period of amenorrhea in 33.3 per cent of cases. It was almost as frequently too small, and sometimes of the expected size. Pre-eclampsia occurred in 8 cases, and eclampsia in one, giving a toxemia incidence of 15.8 per cent. Three other patients had marked proteinuria. Weight loss was noted in 6 cases. Friedman tests were done before evacuation of the uterus in 11 instances and all were positive.

Three of the 57 moles were followed by chorionepithelioma. All of these patients were hysterectomized and survived. All patients in the entire series have been followed up for at least a year, and the only untoward postmolar incident was in a patient who possibly had a second molar pregnancy about 5 months after discharge. There have been 66 pregnancies subsequent to the 57 moles, with 87 per cent eventuating in live births.

It is speculated that the subcapsular hemorrhage occurred more or less concomitantly with delivery, finally to be complicated by rupture of the capsule over the superior surface of the left lobe of the liver with excessive bleeding into the peritoneal cavity.

Abstracts of 5 cases of presumably spontaneous rupture of the liver in pregnancy with hemorrhage into the peritoneal cavity are presented. All 5 instances were in eclamptic patients with no definite history of abdominal trauma. Four cases terminated fatally; one patient recovered following operation. 3 figures.

## HORSESHOE KIDNEY IN PREGNANCY

RUDOLPH BELL

J. Urol., 56: 159-161, 1946

In order to ascertain the best advice to give pregnant women who have horseshoe kidney, a questionnaire was mailed to the members of the American Urological Association. The tabulation of answers to the questions included in the questionnaire produced the following data:

1. Number of patients with horseshoe kidney who have had normal pregnancies, 96.
2. Number of patients with horseshoe kidney who have had complicated pregnancies but went to full term, 49.
3. Number of patients with horseshoe kidney who have had labor induced, 8.
4. Do you consider horseshoe kidney a contraindication to pregnancy? Yes, 23; no, 117; no opinion, 139.

The author presents the case of a woman who presented herself early in pregnancy with horseshoe kidney. Her last menstrual period had been in August, 1939. A urologic investigation was carried out, and in December, 1939, and January, 1940, no pus was noted in the urine and the patient appeared well. On March 20, 1940, she returned complaining of severe bilateral lumbar pain, fever, chills, frequency of urination and dysuria. Urine from the left kidney revealed 4 plus pus and that from the right kidney, 3 plus pus. The patient's course was septic and she continued to be very ill; on March 26, 1940, it was necessary to induce labor. On April 10 she was discharged from the hospital on urinary antiseptics and supportive medication. Infection continued, and on June 4, corrective surgery was performed. When last seen in July, 1945, the patient had experienced no further urinary complications, and had had 2 normal periods of gestation and parturition since the operation.

It is concluded that a high percentage of women with horseshoe kidney have a complicated pregnancy, or have to have labor induced, but that horseshoe kidney is not a contraindication to pregnancy.

epithelioma of the lungs, an enormously enlarged liver filled with metastatic nodules, and small metastatic nodules in the spleen. 10 figures.

## DIABETES IN PREGNANCY

ELISABETH B. WARD

J. Med. Soc. New Jersey, 43: 267-268, 1946

The discovery of insulin has altered the incidence of diabetes in pregnancy cases, since juvenile diabetics now are more likely to reach the child-bearing age, and with insulin, there are fewer cases of sterility and endocrine disorders. Today, wherever there is complete control of the diabetes, maternal risk is largely eliminated, except for the danger from toxemia, which occurs 50 times more frequently in the diabetic than in the non-diabetic.

The author points out that glycosuria is not a criterion for diabetes, in that it is found in about 66 per cent of normal pregnant women. True diabetic glycosuria may be determined by blood sugar determination, tolerance test and the usual diabetic symptoms.

To control the pregnant diabetic completely requires the utmost cooperation between patient and physician. White advises a diet containing 150 to 200 grams of carbohydrate, 2 grams of protein per kilogram of body weight and fat yielding 30 calories per kilogram. Generally, fairly large amounts of carbohydrates are considered advisable because of the excessive excretion of sugar in pregnancy. To utilize this carbohydrate, protamin zinc insulin is given daily. An average of 21 units is suggested for the first trimester and 30 units during the second and third.

In general, the patient should not be allowed to gain more than 2 pounds per month in early pregnancy and 3 pounds per month during the last trimester. Any sudden weight gain is serious, especially in the diabetic, and should be prevented. When a true pre-eclampsia exists, rapid dehydration by means of magnesium sulfate and 50 per cent intravenous glucose is indicated. In addition to sudden weight gain, rise in blood pressure to more than 140/90, albuminuria, headache and epigastric pain are danger signs. If the patient does not respond to ambulatory treatment, hospitalization should not be delayed, since in the diabetic toxemias often become rapidly worse, and danger to the child is greater than in the non-diabetic. Morphine will mask the symptoms of coma in the diabetic, and should be avoided.

White, in a recent study of pregnant diabetics, found that an abnormal rise of chorionic gonadotrophin after the twentieth week predicts in the diabetic premature delivery, stillbirth or neonatal death, and that these accidents are prevented by continuous estrogen and progesterone therapy. Diethyl stilbestrol has been used for this purpose without side reactions.

Spontaneous delivery is now generally preferred, but the fetal heart should be

CHORIO-EPITHELIOMA WITH HERPES GESTATIONIS; REPORT OF  
A CASE

J. M. WHITFIELD, L. SMITH AND R. C. MANSON

Virginia M. Monthly, 73: 257-262, 1946

The authors' purpose in presenting this case is to add another report to the literature, and to record a group of findings which may add to the already accumulated knowledge of one of the unusual types of malignancy.

The patient, aged 34, entered the hospital on September 25, acutely ill and suffering from a diffuse rash which covered the entire body and involved the palms of the hands and soles of the feet. Her last menses had occurred April 1, but no movements had been felt. She had suffered with marked nausea and progressive weakness and had been treated in another hospital for 2 attacks of vaginal bleeding. On August 5 three vaginal cysts had been removed; these showed no trace of malignancy.

The patient had a 10 year old child and 4 years previously had aborted at about the third month of gestation. No fetus was seen at this time and bleeding was extensive.

Examination revealed an emaciated female, vomiting, restless and in pain. Her temperature, pulse and respiration were normal and heart and lungs were negative. There was a generalized symmetrical papulo-vesicular rash with some excoriated and secondarily infected areas. An abdominal mass, apparently the uterus, extended 10 cm. above the symphysis pubis. Laboratory studies showed a white count of 10,500 and hemoglobin of 64 per cent. These figures gradually changed to show an increasing infection and secondary anemia. A Friedman test on September 1 was reported positive.

A diagnosis of herpes gestationis with missed abortion was made and it was decided to interrupt the pregnancy per vaginam. Various drugs failed to accelerate the emptying of the uterus and an x-ray of the uterus showed no suggestion of fetal form. The existence of a pregnancy now being doubtful, the cervix was dilated and portions of a necrotic mass, adherent to the uterine wall, were removed. No cell structure was found definite enough to determine the nature of the growth.

A diagnosis of chorio-epithelioma was made and the abdomen opened. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The pathological report showed a tumor mass, the size of an orange, within the enlarged uterus. Both ovaries were cystic, the left showing solid masses of chorio-epithelioma. Microscopic examination showed chorio-epithelioma which was later classified as Grade 3 malignancy. There was no evidence of abdominal metastasis.

Following operation the skin healed and the patient improved for 2 weeks. On October 15, x-ray examination showed metastatic malignancy filling the lungs; the patient declined progressively and died on November 6. Post-mortem findings included healed lesions of herpes gestationis, metastatic chorio-

glucose tolerance, but have also prevented violent fluctuations in the diabetic state. In other words, during the mid-period of the menstrual cycle when estrogen in the circulating blood is at its peak, the insulin requirement of this patient is much less than it is near and during the menses when the estrogen level is low. Therefore, her insulin requirement was dramatically decreased by the administration of estrogen. Moreover, the administration of large doses of estrogens has tended to stabilize the diabetic state, as shown by the cessation of previously frequent episodes of hypoglycemia and ketosis.

## HEART DISEASE IN PREGNANCY

W. B. STROMME AND KATHERINE KUDER

Am. J. Obst. & Gynec., 52: 264-272, 1946

In the 37,913 obstetric patients seen in the authors' clinic in the past 12 years, there have been 1138 with heart disease, an incidence of 3 per cent. Seven hundred and twenty of these cases are analyzed in the present paper; these represent 3.02 per cent of the 23,858 pregnancies cared for from September 1, 1937 through December 31, 1944. This series is compared with 418 cases seen in the previous 5 years.

According to the New York Heart Association functional classification, 38.48 per cent occurred in Class I, 44.72 per cent in Class II, 10.69 per cent in Class III, and 1.53 per cent in Class IV. The etiologic distribution of heart disease in the present 720 cases was as follows: rheumatic, 91.15 per cent; congenital, 4.31 per cent; hypertensive, 2.22 per cent; paroxysmal tachycardia, 0.42 per cent; syphilitic, 0.28 per cent; kyphoscoliotic, 0.14 per cent; and unknown, 1.53 per cent.

A history of previous disease was given in 61.80 per cent of the total cases of heart disease. Rheumatic fever in one or more of its manifestations occurred in all but 2.43 per cent. As would be expected from the preponderance of rheumatic heart disease, mitral lesions accounted for 78.47 per cent of all valvular lesions. However, the authors are not convinced that it is more dangerous than other valvular lesions. The average length of labor in 260 primiparas with heart disease was 20 26/60 hours, and in 332 multiparas 8 47/60 hours as compared with the normal given by Stander as 18 and 12 hours, respectively. No appreciable difference was noted in the length of labor among the various cardiac classes.

Good treatment rests on proper study and evaluation of each patient. Hospitalization prior to delivery is an important factor in obtaining a low mortality rate in cardiac patients, particularly in the severe cases. The greatest dangers are auricular fibrillation and history of decompensation. In comparing the methods of treatment in the present 720 cases with those in the earlier 418 cases, the authors have noted a trend from cesarean section to forceps deliveries, a

observed closely throughout labor, and at the first sign of fetal distress, instrumental delivery should be considered. Cesarean section should be done for non-diabetic reasons. The newborn must be carefully watched for evidence of hypoglycemia and, if necessary, treated by 10 per cent glucose every 2 hours by mouth or subcutaneously. Postpartum maternal blood sugars must be watched to prevent serious accident, since a change in the insulin requirements often occurs.

## THE INFLUENCE OF OVARIAN ACTIVITY AND ADMINISTERED ESTROGENS UPON DIABETES MELLITUS: CASE REPORT

J. H. MORTON AND T. H. MCGAVACK

*Ann. Int. Med.*, 25: 154-161, 1946

The authors cite evidence for an over-all antagonistic action between the hypophysis and the islets of Langerhans. Hypophysectomy results in marked improvement in the diabetic state of depancreatized animals, and permanent diabetes can be produced by injecting extracts from the anterior pituitary. The administration of sex hormones in large doses is known to exert a suppressive action upon the gonadotropic hormone of the anterior pituitary and upon the growth, the lactogenic, the thyrotropic and the diabetogenic incretions. Evidence has slowly accumulated which shows that diabetes is favorably affected by estrogens in sufficient dosage. The frequency of onset or aggravation of diabetes at the menopause and its response to estrogenic hormones has been observed by several workers. Mazer and Israel emphasize the importance of employing massive doses, such as 10,000 R.U. every fourth day, in order to inhibit anterior pituitary activity. Spiegelman found that the administration of 10,000 R.U. of estrogenic hormone twice a week to 9 diabetic women reduced their insulin requirement.

The case reported in this paper confirms the ability of the clinician to reduce the insulin requirement in diabetes by the administration of estrogen. Primarily, it is of interest because it appears to be the first demonstration in a human of the inhibitory action of therapeutically uninfluenced ovarian function upon the diabetogenic principle of the anterior pituitary.

The patient was first admitted to the hospital at the age of 31, with uncontrolled diabetes. Fluctuations in the patient's own blood and tissue stores of hormone were sufficient to alter her carbohydrate tolerance with every menstrual cycle. She uniformly lost tolerance with the onset of the menstrual flow and regained it at mid-interval. These changes were of sufficient degree to produce coma with menstruation. If diet and insulin were adjusted to prevent such a complication and were not changed again in the middle of the cycle, then hypoglycemic shock invariably occurred.

Relatively large doses of estradiol dipropionate have not only improved her

## PREGNANCY IN A UTERUS BICORNIS

D. W. ROBINSON

Brit. M. J., 1: 836, 1946

A 24 year old primigravida was admitted to the hospital when 38 weeks pregnant. At 12 weeks she had had central abdominal pains, lasting off and on for one month, with 7 days of vaginal bleeding. At the end of the month she passed a small "piece of membrane". On the day prior to hospital admission, while being x-rayed lying on her abdomen, she had experienced severe colicky abdominal pain and vomiting.

On examination, the fetus was found to present by breech; fetal parts and heart were easily detected. There was tenderness above McBurney's point, with no rebound sign. There were shifting dullness in both flanks and tenderness in both loins. The os was closed and there was no vaginal bleeding. In 2 hours the pulse and temperature were elevated, and a tentative diagnosis of acute appendicitis was made.

At operation free blood was found present in the abdominal cavity. The child's head lay among small intestine and was covered with omentum; the breech was partially inside a thin membranous sac, which was seen to be the ruptured right horn of a bicornate uterus. The child was delivered and the right horn removed. After its removal the uterus was nearly like a normal one in shape with both tubes and ovaries in the usual position. But mother and child progressed satisfactorily.

ACUTE POLIOMYELITIS IN PREGNANCY; ITS OCCURRENCE  
ACCORDING TO THE MONTH OF PREGNANCY AND SEX  
OF FETUS

W. L. AYCOCK

New England J. Med., 235: 160-161, 1946

The author finds that comparisons of the percentage of cases of poliomyelitis that occur in pregnant women with the estimated percentage of women of corresponding ages who are pregnant at any given time, as calculated from birth rates, indicate an increased incidence of the disease during pregnancy. In Massachusetts in 1945 there were 54 cases of poliomyelitis. Forty of these were checked as to whether or not the patient was pregnant. The expected number of cases in pregnancy, calculated on this basis, would be 3.102. Actually 10 cases were observed in pregnant patients.

In the author's records there are 236 cases in which the month of pregnancy in which the disease occurred is known, and 9 cases in which it occurred within 23

greater use of local anesthesia, and an evident liberalization in interruption of pregnancies in bad risk cardiacs. Operative deliveries occurred in 29.08 per cent of the 720 more recent cases. Therapeutic abortions were performed in 8.29 per cent of this series, as compared to 2.87 per cent in the earlier group.

On the basis of the present 7-year study, heart disease was found to be the leading cause of maternal deaths at the Lying-In Hospital (24.33 per cent). Its prime position may be said to be due to greater success in controlling infection and hemorrhage. Compared with the previous 5 years, the maternal mortality in cardiac patients has been reduced from 14.18 to 12.64 per 1000 cardiac patients. The mortality in the unregistered group of patients is 7 times that in the registered group. The infant mortality is essentially unaffected by the maternal heart disease. 3 figures.

### HYPERTHYROIDISM IN PREGNANCY TREATED WITH THIOURACIL

S. STROUSE AND C. DRABKIN

J. A. M. A., 131: 1494-1495, 1946

The authors have been able to find reports of less than 10 cases of hyperthyroidism in pregnancy treated with thiouracil—so far without any toxic effects on mother or child. However, since the drug has caused a number of complications, the authors have hesitated to employ thiouracil in such cases, and in all except the case reported in this paper, they have followed older methods of therapy.

The patient, a 33 year old primipara with recurrent hyperthyroidism, was treated with thiouracil for the last 55 days of her pregnancy. She received 0.6 Gm. daily for 28 days, then 0.4 Gm. daily until the day of delivery, with an excellent clinical response. The membranes ruptured spontaneously, the baby presented by breech, and she was not in labor; because of the obstetrical and medical indications a low cesarean section was performed. Both the delivery and the postpartum course were uneventful, and the patient remained well without further treatment.

Clinically, the infant was not quite normal. The blood organic iodine was 10 micrograms per hundred cubic centimeters of plasma (normal 5 to 7), and the cholesterol was 106 mg. Without treatment the infant has now developed into a normal child for its age. Experimental studies of the effect of thiourea on pregnant rats indicate the possibility of damage to the offspring, with characteristic thyroid hyperplasia and retardation of development. The present case report corroborates experimental studies on the possible harmful effect of thiouracil in pregnancy.

# PATHOLOGY OF LABOR AND PUERPERIUM

## RUPTURE OF THE UTERUS

A. H. DINDIA AND V. J. TURCOTTE

Ohio State M. J., 42: 736-738, 1946

Five cases of rupture of the uterus are presented, and these cases occurred within a period of 20 months within 4 hospitals. They may be summarized briefly as follows:

Case I: The patient was a 30 year old gravida IV and para III at term. Twenty hours after admission to the hospital she was fully dilated, was taken to the delivery room and was given 3 minims of pituitrin. A living child was delivered in 10 minutes, with considerable blood loss. One hour after delivery the patient complained of lower abdominal pain and the pulse was imperceptible. She was given oxygen, ephedrine and 500 cc. of plasma. No diagnosis was made, and the patient expired  $4\frac{1}{2}$  hours following delivery. Postmortem examination revealed a transverse laceration, 14 cm. in length, in the lower uterine segment.

Case II: The patient was a 38 year old gravida IV and para IV at term, whose membranes had ruptured 4 hours previously. Shortly after admission she began to have irregular weak contractions and was given 4 doses of 3 minims of pituitrin within 4 hours. After the third dose she went into active labor. Five hours following the first dose of pituitrin the patient had severe abdominal pain and some vaginal bleeding and went into shock; pulse, blood pressure and fetal heart tones were unobtainable. One hour following uterine rupture laparotomy was performed with the extraction of a dead infant. There was a rent, 12 cm. in length, in the anterior wall of the lower uterine segment. The rent was sutured, transfusion given, and the patient recovered.

Case III: The patient was a 31 year old gravida VII and para VI at term; the membranes had been ruptured one hour and she was not in labor. Twelve hours after admission she was still not in labor and was given 3 minims of pituitrin every half-hour for 4 doses, resulting in the establishment of uterine contractions. These lasted only one hour and she was given 4 more doses of 3 minims of pituitrin. She went into active labor, and 24 hours after the first attempt to induce labor she complained of severe lower abdominal pain, became cyanotic and dyspneic, and there was a moderate amount of vaginal bleeding. A stillborn infant was delivered through the vagina, and shortly thereafter the patient went into shock. She was given plasma, adrenalin, coramine and oxygen, and died 25 hours after the first dose of pituitrin. Autopsy revealed 2 lacerations, 5 cm. in length, beginning at the upper edge of the cervix and extending into the lower uterine segment.

Case IV: The patient was a 38 year old gravida IV and para IV at term. Following admission the contractions became irregular and decreased in in-

days after delivery, which is within the range of the incubation period of this disease. There is no indication of a tendency for the disease to occur at any specific period in pregnancy. However, there are indications that there is a tendency for the disease to occur in the first trimester in women who are carrying a male fetus and in the third trimester in women who are carrying a female fetus. Thus, of 42 cases in which both the month of pregnancy in which the disease occurred and the sex of the child are known, there were 8 women with male infants and one woman with a female infant in the first trimester, equal numbers of infants of both sexes in the second trimester, and 15 women with female infants and only 4 with male infants in the third trimester.

Confirmation of these findings would establish a causal relation between pregnancy and poliomyelitis. Also, it would afford a basis for the elucidation of physiologic or endocrine factors involved in poliomyelitis. Furthermore, such a biphasic phenomenon may reflect physiologic factors in pregnancy with a male or female fetus.

agreed that this hormone does produce the action we want in primary uterine inertia if only its administration could be rendered safe. Can this be done?

At the present writing this question must be answered in the negative, but it can be rendered much safer (and probably as safe as some of the methods mentioned above) if the following regulations are rigidly followed:

1. The case must be one of real uterine inertia, primary in character, with labor practically at a standstill and progress nil.

2. The patient must be actually in labor, not in false or prodromal labor. The only valid evidence of true labor is progressive effacement and dilatation of the cervix. Although this process may have come to a standstill, it must have progressed to the extent of 3 or 4 cm. dilatation. One of the commonest mistakes in obstetrics is to try to "push" labor in patients who are not in labor at all; pituitary extract will only lead to trouble in such cases.

3. There must be no mechanical obstruction to easy delivery as attested by every type of evidence possible, including x-ray study of the pelvis and fetal skull. Unless the latter is done an occasional instance of midpelvic contraction or of brow presentation may be overlooked.

4. Patients of great parity (paras 4 and over, let us say) must not be given pituitary extract because their uteri rupture more readily than those of women in the lower parity brackets.

5. The condition of the fetus must be good as evidenced by a regular heart beat and absence of meconium-stained liquor amnii. A dead fetus is, of course, no contraindication to pituitary extract.

6. The obstetrician must observe and time the first contraction after the administration of the drug, and give inhalations of ether if it lasts longer than three minutes.

7. *The initial dose must not exceed  $\frac{1}{2}$  minim.* This dosage should not be exceeded unless it is clear that no improvement in pains whatsoever ensues. In the latter event it may then be increased to 1 minim but under no circumstances should more than 1 minim be given at a time. A period of 30 minutes must intervene between injections.

8. When in doubt as to whether a given case meets the above criteria, do not give pituitary extract.

Coming back to the above paper it may be noted in the first place that the dosage of pituitary extract employed (3 minims) was 6 times that recommended as the initial dose in the foregoing regulations; and secondly, that all four patients who suffered rupture of the uterus in labor were Para IV or over, that all were at least 30 and 2 were 38 or more. There can be no question but that these patients in the upper parity-age brackets are especially disposed to uterine rupture from all causes.—Ed.)

## THE ASPIRATION OF STOMACH CONTENTS INTO THE LUNGS DURING OBSTETRIC ANESTHESIA

CURTIS L. MENDELSON

Am. J. Obst. & Gynec., 52: 191-205, 1946

Sixty-six cases of aspiration of stomach contents into the lungs during obstetric anesthesia are analyzed. The incidence of this complication was 0.15 per cent in 44,016 pregnancies at the New York Lying-In Hospital from 1932 to 1945. The significant data in the 66 cases are summarized in Table I. The incidence of prolonged labor was somewhat higher than that of the total clinic population, which is 10 per cent.

tensity. She was given 3 minims of pituitrin at 20 minute intervals for 3 doses. One hour after the first dose she went into active labor, complained of severe abdominal pain and had a moderate amount of vaginal bleeding. She became cyanotic with a weak and rapid pulse. Adrenalin, caffeine, sodium benzoate, coramine and oxygen were given. The patient expired 3 hours after the first dose of pituitrin. Necropsy revealed a rent, 12 cm. in length, extending to about 3 cm. distal from the lower uterine segment.

Case V: The patient was a 30 year old gravida III and para III at term. Four hours after admission she was delivered spontaneously of a living child, and following delivery she received 1 cc. of pituitrin. The placenta failed to be delivered, and a gloved hand inserted into the uterus found the placenta adherent to the fundus and a rent in the left side of the uterus. The patient went into shock, and after this was treated a total hysterectomy was performed. The patient recovered. The rent extended from the lower uterine segment to the external os of the cervix.

DeLee has stated that the indiscriminate use of posterior pituitary preparation is one of the 4 major causes for the persistently high maternal and fetal death rates in the United States. It is noteworthy that in 4 of the present cases pituitrin was used during the first or second stage of labor. The authors conclude that the prognosis is influenced by the amount of time elapsing between rupture and the establishment of proper treatment. 1 figure.

(Rupture of the uterus due to pituitary extract is not a condition which practitioners rush to put into print, and as a result the recorded cases of this accident represent only a small fraction of those which actually occur. This forthright paper is therefore most welcome.

There is an authoritative body of opinion which maintains stoutly that pituitary extract should never be given in the first and second stages of labor and the validity of this teaching is well attested by such cases as are reported above. However, uterine inertia also takes its toll in terms of intrauterine infection, maternal exhaustion, Dührssen's incisions and cesarean section; and every obstetrician when confronted with a case of intractable primary inertia, has felt the need for a dependable but safe uterine stimulant. The many attempts to moderate the action of pituitary extract, such as Hofbauer and Horner's nasal pituitrin, thymophysin and Dieckman's pit-sulfonate all point to the fact that such a need does exist.

What are we to do when faced with a stubborn case of primary uterine inertia, a case in which there is no disproportion but in which, after countless enemata, walking, etc., have failed, and hours and even days go by with the cervix still stationary at 3 to 5 cm.,—all because of poor pains? Obstetricians would answer this question in various ways: some would advise more time, perhaps with intravenous fluids occasionally and morphine now and then to provide periods of rest; others might try calcium gluconate possibly; a few might lean to Dührssen's incisions provided the cervix is 6 cm. or more dilated; while still others would consider cesarean section. All these obstetricians would regard their program as safer than pituitary extract and, as indicated above, their fear of this oxytocic is well grounded.

On the other hand, there is a group—a much larger group than is generally realized—who would employ pituitary extract in such a case. And what are we to say to them? Condemn everlastingly the use of pituitary extract before the birth of the baby? This attitude was taken by the late Dr. DeLee and others but has proved of dubious teaching efficacy because there are too many practitioners who have had too many good results with pituitary extract (and too few accidents) for any such general ban to be acceptable. Moreover, it must be

picture was invariably that of obstruction as observed in the human, regardless of whether acid or neutral material was used. Complete obstruction caused suffocation and incomplete obstruction produced massive atelectasis.

Following aspiration of liquid containing hydrochloric acid the animals developed a syndrome similar in many respects to that observed in the human following liquid aspiration. Cyanosis and labored respirations developed immediately, but death often ensued within minutes to hours. The pathologic findings indicate that this syndrome is due to the irritative action of hydrochloric acid, which produces bronchiolar spasm and a peribronchiolar exudative and congestive reaction. Following aspiration of neutral liquid, the animals went through a brief phase of labored respirations and cyanosis, but within a few hours were apparently back to normal.

The author concludes that gastric retention of solid and liquid material is prolonged during labor, and that aspiration of vomitus into the lungs may occur while the laryngeal reflexes are abolished during general anesthesia. Bronchial configuration favors right-sided aspiration. However, massive aspiration readily involves both lungs. Aspiration of solid material produces the classical picture of laryngeal or bronchial obstruction. Aspiration of liquid produces an apparently hitherto unrecognized asthmatic-like syndrome with distinct clinical, roentgenologic and pathologic features.

Aspiration of stomach contents into the lungs is preventable. The dangers of this complication as an obstetric hazard may be avoided by: (a) withholding oral feeding during labor and substituting parenteral administration where necessary; (b) wider use of local anesthesia where indicated and feasible; (c) alkalinization of, and emptying the stomach contents prior to the administration of a general anesthetic; (d) competent administration of general anesthesia with full appreciation of the dangers of aspiration during induction and recovery; (e) adequate delivery-room equipment, including transparent anesthetic masks, tiltable delivery table, suction, laryngoscope, and bronchoscope; and (f) differential diagnosis between the two syndromes described and prompt institution of suitable therapy. 20 figures.

The character of the aspirated material was recorded [in 45 cases; in 40 cases it was liquid and in 5 it was solid. The 5 patients who aspirated solid material exhibited obstructive reactions. Three of these had complete obstruction; 2 died of suffocation and the third recovered after coughing up the obstructing material. These 5 patients exhibited the classical picture of massive collapse with cyanosis, tachycardia, dyspnea, evidence of mediastinal shift and consolidation. A very different type of reaction was observed in the 40 patients that aspirated liquid material. This type of reaction is similar to an acute asth-

TABLE I  
*Analysis of 66 cases of aspiration*

Prolonged labor,	30 hours or over.....	9 or	14%
Type of delivery,	Normal spontaneous.....	29	44%
	Cesarean section.....	14	21%
	Operative other.....	23	35%
Anesthesia,	Gas, oxygen, ether.....	66	100%
Aspiration,	Recorded at delivery.....	45	68%
	solid.....	5	
	liquid.....	40	
	Subsequently diagnosed.....	21	32%
	Obstructive reaction.....	5	8%
	suffocation.....	3	
	massive collapse.....	2	
	Asthmatic-like reaction.....	61	92%
	Recorded.....	55	83%
Cyanosis,	Pulse over 110 per minute.....	66	100%
Tachycardia,	Respirations over 30 per minute.....	66	100%
Dyspnea,	Diffuse.....	15	23%
Chest pathology,	Right only.....	51	77%
	Left only.....	0	0%
	Febrile.....	20	30%
Morbidity,	chest.....	8	
	pneumonia.....	6	
	abscess.....	2	
	other.....	12	
	Sulfonamides.....	14	21%
Chemotherapy,	Penicillin.....	3	5%
	Both.....	2	3%
	Immediate.....	2	3%
Deaths,	Later.....	0	0%

matic attack. Cyanosis, tachycardia and dyspnea developed, but there was no massive atelectasis or mediastinal shift. Auscultation revealed numerous wheezes, rales and ronchi. High pulse and respiratory rates were common. Evidence of cardiac failure frequently appeared, and occasionally culminated in pulmonary edema.

A series of animal experiments were undertaken to determine the pathology of these 2 different aspiration syndromes. Various materials were introduced into the lungs of adult rabbits. Following the aspiration of solid undigested food the

to the practice prevailing in many countries, notification in England and Wales does not mean notification of proved gonococcal cases, but of purulent conjunctivitis from any cause. This is important, since other organisms than the gonococcus may be equally responsible for disastrous results.

Early results with the sulfonamides were somewhat confusing, as the derivatives at that time were not devoid of toxicity and were not so effective against a variety of causal organisms as the later ones. By 1940 the position had clarified sufficiently to permit the routine use of oral sulfonamides in cases of ophthalmia neonatorum. In a preliminary series of 273 cases treated at White Oak Hospital with sulfapyridine, 61.9 per cent of the infants were cured within 8 days, as compared with 15.2 per cent of those treated with classical methods. A second series of 333 cases treated with more standardized dosage showed a considerable proportion with clinical cure within one to 3 days. Ultimately, sulfamethazine was chosen as the standard drug. In no case did corneal complications arise during the course of treatment. Of 20 babies admitted with corneal ulceration, in only 3 was the residual scar sufficiently dense to arouse fear as to the ultimate state of vision.

Penicillin therapy proved remarkably successful. Where the sulfonamides cleared the condition within days, penicillin cleared it within hours. The most consistent results are obtained when the concentration of penicillin is 2500 units per cc. Equally important is the frequency of application; in the last 72 cases treated at White Oak Hospital, penicillin has been instilled at intervals of one minute and usually all pus can be suppressed within 30 minutes. Thereafter, a simple conjunctivitis remains which heals within 2 to 3 days.

The author discusses the etiology and prevention of ophthalmia neonatorum. In a series of 737 consecutive cases admitted to White Oak Hospital, only 180 were found to be caused by the gonococcus. Various staphylococci were responsible for 271 cases, bacilli for 119 cases, and streptococci, pneumococci, and other coccal organisms for a small quota of cases. In 126 cases no organism was found. It appears that some 15 per cent of all cases are virus in origin. Thus, while the Cr  d   procedure, compulsory notification and recent developments in chemotherapy have diminished the significance of ophthalmia neonatorum, it is now important to study intensively the various maternal infections that may lead to the affection and, through public health machinery, to provide adequate antenatal treatment of such infections.

## OPHTHALMIA NEONATORUM—A HISTORICAL R  SUM   AND PRESENT STATUS IN THE UNITED STATES

HARRY WAIN

Sight-Saving Rev., 15: 196-201, 1945

While accurate descriptions of gonorrhea as a genital disease exist in our earliest medical records, little or no mention is made of either gonorrheal or any

## THE NEWBORN

### OPHTHALMIA NEONATORUM IN ENGLAND, 1884-1944

ARNOLD SORSBY

Sight-Saving Rev., 15: 187-195, 1945

A survey conducted by the Ophthalmological Society of the United Kingdom in 1884 showed that between 30 and 41 per cent of inmates of schools and institutions for the blind had been blinded by ophthalmia neonatorum. In 1922 the Ministry of Education found that 28.5 per cent of children at schools for the blind were blind from this affection. A parallel investigation in 1944 showed that ophthalmia neonatorum was responsible for only 9.2 per cent of blindness. Thus, while there was some decline in the incidence of blindness from ophthalmia neonatorum between 1884 and 1922, there was a considerably large decline between 1922 and 1944. Between 1941 and 1944 only 3 infants are known to have been blinded from this condition in England and Wales.

The author credits the decline of blindness from ophthalmia neonatorum to 3 factors. First was the application of the Credé technique which was developed in the eighties of the past century. Second was the formation of a movement by ophthalmic surgeons and local authorities to provide adequate facilities for treatment. In 1914 a statutory order made ophthalmia neonatorum a notifiable disease, imposing upon local authorities the obligation of seeing that adequate treatment was available for affected infants. There is much to indicate that it was this statutory enactment which initiated the decline in the incidence of ophthalmia neonatorum. The average number of babies reported blind from the disease in England and Wales per year during the period from 1934 to 1937 was 7. Blindness from this condition was thus reduced from a mass problem to occasional tragedies. However, that ophthalmia neonatorum was still a formidable affection is seen from the fact that impaired vision resulted in an average of about 31 infants per year from 1934 to 1938.

The almost total elimination of blindness from ophthalmia neonatorum today is attributed to the use of the sulfa drugs and penicillin in treating the disease. The influence of such therapy began to exert itself in about 1940 when the sulfonamides replaced classical methods of treatment, reducing the duration of ophthalmia neonatorum from weeks to days, greatly eliminating the chance of corneal involvement.

In the Order of 1914, making ophthalmia neonatorum notifiable, the condition was defined as a "purulent discharge from the eyes of an infant commencing within twenty-one days from the date of its birth." In 1936 the Order was modified, when the duty of notification was laid exclusively on the medical attendant; the duty of a midwife was now to summon medical assistance in a case of "any inflammation or discharge from the eyes, however slight." In contrast

states. These laws vary in different states, but in general they require the reporting of cases, free distribution of silver nitrate and the use of preventive drops. According to 1945 statistics, all 48 states and the District of Columbia require the reporting of cases, and all but 2 require the use of a prophylactic in the eyes of the newborn.

For years, the treatment of ophthalmia neonatorum was difficult and uncertain. With the advent of the sulfa drugs, treatment was greatly improved, and the discovery of penicillin has revolutionized the treatment so that now a cure is quick and simple if penicillin is used in time.

Thus, ophthalmia neonatorum, once responsible for 30 per cent of all cases of blindness, is now responsible for only 2.4 per cent of blindness. However, to be absolutely safe from the danger of blinding gonorrheal ophthalmia, gonorrhea itself must be eradicated. Even if the prophylactic drops are used, an infected mother may carry infection to the child after birth by means of contaminated fingers or washcloths. To eliminate the hazard of ophthalmia neonatorum, whether caused by the gonococcus or any other organism, it will be necessary to conquer these germs.

## OPHTHALMIA NEONATORUM

A. SORSBY

Practitioner, 157: 66-68, 1946

Most series of cases of ophthalmia neonatorum show that the condition is caused by a great variety of organisms, and often the gonococcus is not the predominant causal organism. It was responsible for about 25 per cent of 737 cases referred to in this paper, while *Staphylococcus aureus* accounted for about 35 per cent and the meningococcus, pneumococcus, streptococcus and other coccal organisms each contributed a small percentage. Bacilli were responsible for about 20 per cent. In some 10 to 20 per cent of cases no micro-organism can be found, and these are examples of ophthalmia neonatorum due to a virus infection. While this virus has not been isolated in culture, its existence has been demonstrated by animal inoculation, and by the presence of inclusion bodies in the conjunctival epithelium—a finding responsible for the designation of inclusion ophthalmia neonatorum, or inclusion blenorrea.

The essential measure of prophylaxis in this affection is the treatment of maternal infection during pregnancy. The more immediate method of prophylaxis associated with the name of Credé is immensely valuable, but has distinct limitations. The author recommends that 20 per cent argyrol be instilled into the baby's eyes rather than 1 per cent silver nitrate.

Two alternative procedures are available in the modern treatment of ophthalmia neonatorum: sulfonamide therapy and penicillin therapy. The

other type of ophthalmia neonatorum. However, Aetius, writing in about the year 500, mentioned ophthalmia neonatorum in his system of medicine. It took a long time to discover that gonorrhea was a cause of ophthalmia neonatorum. In 1750, S. T. Quellmatz discovered the cause to be in the vaginal discharge of the mother at the birth of the child, but unfortunately this discovery was not accepted. In 1807, Dr. Benjamin Gibson of England reported his observations that the child's eyes were infected from the mother's gonorrheal condition. He advised: (1) remove the disease, if possible, in the mother during pregnancy; (2) if this cannot be done, remove artificially as much of the discharge as possible from the vagina at delivery; and (3) at all events, pay particular attention to the child's eyes, washing them immediately after delivery.

Other workers proved experimentally that ophthalmia neonatorum was commonly caused by gonorrhea. Vetch, in 1820, inoculated the canal of the penis in a male patient with pus from a baby's eyes and produced gonorrhea. Pauli of Landau, in 1854, introduced pus from a baby's eyes into the vagina of a prostitute and produced gonorrhea. However, the truth was accepted slowly, and it was not until 1879 when Albert Neisser of Breslau, Germany, discoverer of the gonococcus, announced that gonorrhea germs were frequently to be found in the secretions from "babies' sore eyes", that it was proved conclusively that the gonococcus was a blinder of babies.

One of the greatest triumphs of preventive medicine was achieved by Dr. Karl Sigmund Franz Credé, professor of obstetrics and gynecology at the University of Leipzig, Germany, who, in the years from 1880 to 1882, systematized and published a method of preventing this disease. In his own words, the method was as follows: "The eyelids were gently separated by an assistant, and by means of a glass rod a single drop of the solution (2 per cent silver nitrate) was placed in each eye. For twenty-four hours after the application, the eyes were cooled by means of a linen fold, soaked in salicylic acid (2:100) laid over them." In Credé's hospital in the year 1874 there were 323 births with 45 cases of gonorrheal ophthalmia, or 13.6 per cent, and, in 1882, in 260 births where the method was used, only one case developed, or 0.5 per cent.

Ignorance, carelessness and prudery on the part of doctors, midwives and the public held back the universal use of Credé's method. Many doctors who used the method on charity patients were hesitant to use it on their private patients, lest they imply that their patients had gonorrhea. The slowness with which the medical profession adopted Credé's method is revealed by an investigation in Boston in 1909 (27 years after Credé's demonstration of his method). Of 97 doctors visited who had large obstetrical practices, only 27 always used a prophylaxis, 40 seldom used any, and 28 never used a recognized preventive. The situation was even worse where a midwife attended; 9 out of 10 midwives were incompetent and unclean, yet, in 1904, records showed that 86 per cent of all reported births in the United States were attended by midwives.

Legislation for the control of ophthalmia started in the United States in New York State in 1890. Dr. Lucien Howe was a leader in the fight for this legislation, and the law became known as the Howe Law, and was copied by other

states. These laws vary in different states, but in general they require the reporting of cases, free distribution of silver nitrate and the use of preventive drops. According to 1945 statistics, all 48 states and the District of Columbia require the reporting of cases, and all but 2 require the use of a prophylactic in the eyes of the newborn.

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Two alternative procedures are available in the modern treatment of ophthalmia neonatorum: sulfonamide therapy and penicillin therapy. The

sulfonamides are useless when applied locally, but are highly effective by mouth. Sulfamethazine, 0.25 gm., is given as the initial dose and administration is continued in doses of 0.125 gm. every 4 hours, day and night, until 48 hours after a clinical cure is obtained. With this treatment, swelling of the lids generally subsides within 12 hours, and purulent discharge disappears within 24 hours. Some 40 per cent of cases are cured within 3 days, and 90 per cent are cured within 8 days.

Unlike the sulfonamides, penicillin remains effective in the presence of pus and may be given locally; furthermore, cures are even more rapid and dramatic with penicillin than with the sulfonamides. Two drops of penicillin, 2500 units per cc., are instilled into the eye every minute for 30 minutes. The drops are continued at 5-minute intervals for half an hour. Thereafter, penicillin is continued at half-hourly intervals for 6 hours, then at hourly intervals for 12 hours. As a rule, the eyes are normal by this time.

A striking feature of both sulfonamide and penicillin treatment is their efficiency over the entire range of causal organisms, including the virus of ophthalmia neonatorum. Gonococcal cases respond somewhat more quickly than non-gonococcal cases to oral sulfonamide treatment, and those due to diphtheroids possibly respond rather less readily to local penicillin therapy than the cases due to other organisms.

## THE EARLY FAILURE OF BREAST FEEDING; A CLINICAL STUDY OF ITS CAUSES AND THEIR PREVENTION

HAROLD WALLER

Arch. Dis. Childhood, 21: 1-12, 1946

The main principle set forth in this paper is that the successful start of breast feeding depends on milk pressure within the breasts not rising to an excessive height. If the pressure does rise, and if it is not speedily lowered, there results a rapid decline in milk production because of alveolar distension and compression of the secreting cells. The author claims that this is the chief reason for the statement by so many women that their milk fails soon after they get up from childbed.

The relative lack of statistics on the duration of breast feeding and on detailed cause for failure is pointed out. A recent British government publication is quoted as saying that about 80 per cent of babies leave the hospital wholly breast fed and that 95 per cent of the babies born on the district are wholly breast fed when the midwife leaves. Whether the infants are home or hospital born, it appears that only some 50 per cent are breast fed at the end of 3 months, and 40 per cent at the end of 6 months. In a group of 436 primiparous women seen consecutively at infant welfare centers in East London it was found that 28 per

cent had ceased to breast feed by the end of one month, 38 per cent before 2 months, and 42 per cent before 3 months, the majority therefore ceasing in the first 2 months.

The frequency of high milk pressure at the beginning of the first lactation is attributed generally to certain anatomic defects of the nipples and the terminal ducts, a claim for which there is ample clinical evidence but which needs confirmation by other and more exact means.

The author describes a controlled experiment which tests this hypothesis. One hundred women were prepared for their first lactation as "pupils" and 100 other women served as "controls". The pupils were taught the daily manual removal of colostrum during the last 3 months of pregnancy; the control group did not employ this practice, but otherwise the treatment during the lying-in period was identical for the 2 groups. Excessive milk pressure occurred in 25 per cent of the pupils and in 56 per cent of the controls. At the end of 6 months 83 per cent of the former were still successfully breast feeding, as compared with only 42 per cent of the latter. For this result it is suggested that the preliminary removal of colostrum facilitated the initial outflow of milk by stretching and enlarging the terminal part of the duct system.

The method of manual expression taught to the pupils consists of 2 separate movements. The first is a compression of the whole breast with both hands, starting as its margins and continuing to the areola. This is repeated 10 to 12 times to impel colostrum from the finer into the larger ducts and lacteal sinuses. The second movement, designed to empty the sinuses, consists of repeatedly pinching the sinuses between thumb and forefinger.

Since the experiment reported above, the preparatory technique has, as far as possible, been taught to all primigravidae and to those who have had experience of lactation difficulties. Replies to a questionnaire sent to 300 primiparae delivered consecutively in the early months of 1945 showed that 79.3 per cent were fully breast feeding at 6 months. In 5 per cent of the series stilbestrol was used to control milk tension. 5 figures.

## PENICILLIN IN THE TREATMENT OF NEONATAL SEPSIS

F. M. B. ALLEN, J. E. MORISON AND W. R. RUTHERFORD

Arch. Dis. Childhood, 21: 19-22, 1946

A diagnosis of neonatal sepsis was made in 71 cases and every alternative case was treated with both penicillin and sulfadiazine. The remaining cases, which served as controls, received sulfadiazine alone. A study of the 61 cases which were suitable for analysis failed to show that penicillin increased the recovery rate, or influenced either the duration of the illness or the severity of decline in body weight.

In certain well-defined conditions, such as staphylococcal infections, and probably in some cases of primary bacterial pneumonia, penicillin possesses some advantage over sulfadiazine. However, it would seem that the organisms responsible for much of the sepsis in the newborn are no more responsive to penicillin than to sulfadiazine.

In regard to respiratory infection, which was present in a high incidence of cases, it would be assumed that, if the bacteria concerned were pathogens derived from the respiratory tract of adults, a high proportion would be sensitive to penicillin. It is possible, however, that the organisms are derived from the normal flora of the nose and throat of the newborn, and that toxins acting on immature structures, associated virus infection or some other factors, depress the normal defense mechanisms which include the protective reflexes guarding the respiratory tract.

A few cases, chiefly of staphylococcal infection, were thought to benefit in a further group of 18 cases treated without controls. In this group of cases which responded to penicillin the infections resembled those of later childhood or adult life which are amenable to penicillin.

## CONGENITAL CARDIAC DEFECTS ASSOCIATED WITH MATERNAL RUBELLA

L. P. WINTERBOTHAM

M. J. Australia, 2: 16-19, 1946

At the Blind and Deaf School of Brisbane in 1945 there were 121 pupils on the roll; the number of new pupils entered each year averages 7, but last year a sudden influx occurred when 48 new pupils (born in 1938) were enrolled. A history of maternal rubella was obtained in 34 cases. Of the 121 children on the roll, 116 were available for investigation. None of the blind children examined had any heart lesion, but of 109 deaf children, 19 were so affected (17.4 per cent).

Those with cardiac defects may be classified as follows: (1) 11 of the 34 denoted above, with a history of maternal rubella; (2) 8 of 75, in whom no history of rubella could be obtained; (3) 12 of 47 children born in 1938; (4) 5 of 43 children born before 1938; (5) 2 of 19 children born after 1938.

The 2 principal outbreaks of rubella in Queensland in recent years occurred in 1937 and 1940. There was a considerable increase in the number of cases of congenital deaf-mutism in 1938, and an increased number of deaf children born in 1941 are now registering at the School for Blind and Deaf Children. In 1941 deaths from congenital heart disease reached the highest figure so far recorded for Queensland.

In New South Wales there was a tremendous increase in the number of children absent from school because of rubella in 1940; this coincides with a large

increase in the number of admissions to the New South Wales school for the deaf of children born in 1941.

In Victoria there was considerable increase in the number of admissions to the school for deaf children whose birth occurred early in 1941. There were epidemics of rubella during 1939 and 1941. In both years increases in infantile cardiac mortality occurred.

Epidemics of rubella are stated to recur every third or fourth year, and it is a remarkable fact that practically every fifth year for the past 42 years there has been a wave of increase in the number of deaf children occurring in Queensland.

The author suggests that valuable evidence could be collected if head teachers of state and denominational primary schools obtained from parents enrolling their children information as to whether the mothers whose period of pregnancy corresponded with rubella epidemics had contracted this disease during the first 4 months of pregnancy. Such information concerning healthy children would be valuable, and subsequent examination of such children should be made with particular reference to the cardiac system and intelligence quotient.

## TETANUS OF THE NEWBORN. TWO CASES CURED WITH PENICILLIN

R. C. NEGRO AND M. TOLOSA

Arch. de pediat. d. Uruguay, 17: 289-303, 1946

Tetanus of the newborn, caused by *Clostridium tetani*, is now rare, due to modern methods of obstetric asepsis, but it is still frequent in some countries where unsanitary conditions prevail. The portal of entry for the microbe is usually the umbilical cord; infection may follow birth injuries, circumcision wounds or vaccination scarifications. When the umbilicus is the portal of entry, there are frequently pyogenic organisms which result in mixed infection and local inflammation.

The duration of the incubation period is usually from 3 to 10 days. Restlessness, irritability and crying precede the muscular contractions, which are the main symptom. Trismus is always present, becoming more pronounced and persistent. Later, the contracture becomes generalized, advancing to the trunk, extremities and abdomen. The contracture increases and occurs in attacks of varying duration. During these attacks the child presents opisthotonus, redness of the face, white froth at the mouth, accelerated pulse and respirations, and sometimes apnea. The temperature may or may not be elevated. Usually there is evidence of umbilical infection. Although recovery may occur, death due to asphyxia, inanition, or infectious complications is the rule.

The prognosis is grave; mortality rates vary from 56.6 to 100 per cent. The longer the incubation period, the more favorable the outlook. A high temper-

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## OPERATIVE OBSTETRICS

### DISPUTED INDICATIONS AND TECHNICS FOR CESAREAN SECTION

E. G. WATERS

New England J. Med., 234: 849-853, 1946

It is the purpose of this paper to discuss the most frequently disputed indications for cesarean section, and to state the position currently arrived at in respect to them and to the technics preferred.

In the author's clinic, obvious fetopelvic disproportion in primiparas raises no dispute as to elective cesarean section, but these cases form a distinct minority. The majority of cases constitute the "borderline pelvis" group. With regard for those factors which cannot be determined in advance of labor (size, shape and moldability of fetal head, physiologic relaxation of pelvic joints, thickness and tension of nonosseous pelvic structures, character of uterine contractions, time factor in dilatation and effacement of the cervix, etc.), sufficient labor is allowed to borderline cases to permit the primiparous patient to demonstrate her capability for vaginal delivery.

Cesarean section is no longer performed in cardiac cases unless there is an obstetric indication for the operation. The incidence of decompensation has been reduced from 22.3 to 2.5 per cent, and the mortality from 3.5 to 0.6 per cent, largely through competent medical care and the elimination of operative interference for other than obstetric indications.

In regard to abruption of the placenta or premature separation of the placenta, cesarean section would not be indicated in a multiparous patient with an effaced cervix approaching full dilatation or in any patient with shock or hemorrhage, without first re-establishing blood volume, overcoming anoxia and combating shock. On the other hand, it is indicated when complete abruption occurs with the cervix and birth tract unready for delivery, when means are at hand for combating shock and blood loss. The individual case determines the policy to be followed.

The author's attitude toward pre-eclampsia and eclampsia is conservative. Cesarean section is not performed in eclampsia unless the patient is controlled and operable. Patients with pre-eclampsia are treated medically unless the toxemia is progressive or recurrent, in which event termination of the pregnancy is advised, since babies delivered early in a severely toxemic pregnancy have a better chance than those carried nearer to term, and damage to maternal structures parallels the duration of the toxemia. Cesarean section was performed in 61 (6.9 per cent) of 879 cases of mild pre-eclampsia, with no maternal deaths. Section was done in 26 (22 per cent) of 117 cases of severe pre-eclampsia; thus, the need for cesarean section in severe pre-eclampsia is 3 times as great as in the mild group. Cesarean section was performed in 20 (8 per cent) of 236 cases of

ature, frequent and severe attacks and intercurrent infections render the prognosis unfavorable. The diagnosis is established by the appearance of the umbilical cord and wound, trismus, rigidity, absence of clonic contractures, absence of involvement of the ocular muscles and of general paralysis, and the presence of *Cl. tetani*. The condition must be differentiated from interstitial encephalitis of the newborn, paresis, intracranial hemorrhage, meningitis and tetany.

Antitetanus and sedatives have failed to reduce the mortality; specific serum is valuable prophylactically, but has little curative effect. However, the results with penicillin have been excellent. In the authors' 2 cases mixed treatment was given (antitetanus serum subcutaneously and intramuscularly, 5000 units daily for the first 2 days, and penicillin intramuscularly, 10,000 units every 3 hours for the first 10 to 12 days, and then half the dose until symptoms had completely disappeared). Luminal and chloral hydrate were used as sedatives. Magnesium sulfate has produced excellent results; its respiratory depressant effects may be avoided by injecting calcium gluconate.

Gentleness in handling the infant and guarding against such accidents as suffocation due to regurgitation, or severe cyanosis, are important. Nutrition must be maintained and dehydration prevented.

In both of the authors' cases the symptoms began on the eighth day of life; recovery ensued in 55 and 24 days, respectively.

## DIET OF MOTHER AND HYDROCEPHALUS IN INFANT RATS

L. R. RICHARDSON AND A. G. HOGAN

Federation Proc., 5: 238-239, 1946

The data presented in this paper indicate that hydrocephalus in infant rats was due to a deficiency of an unidentified nutrient, which is present in a liver eluate and in many natural foodstuffs. It is suggested that hydrocephalus in other animals, including man, may be due to an inadequate diet.

Group I, consisting of 230 female rats, received a diet, 100 grams of which contained 3000 I. U. of vitamin A, 425 I.U. of vitamin D, 2.5 mg. each of alphatocopherol and of 2-methyl-1, 4-naphthoquinone, 1 mg. each of thiamine, riboflavin and pyridoxine, 4 mg. of calcium pantothenate, 5 mg. of nicotinic acid, 100 mg. each of choline, inositol, and p-aminobenzoic acid, and 20 mcg. of biotin. Group II, consisting of 54 females, received a mixture of the diet given to Group I and an eluate of a fuller's earth adsorbate of a liver extract. A total of 1756 infant rats in Group I survived at the weaning age of 28 days, and in addition there were 30 which developed hydrocephalus between the ages of 10 and 24 days. Of these 30, only 2 survived as long as 28 days. A total of 1020 infant rats in Group II survived until they were weaned and several thousand young were reared in the stock colony, with no indication of hydrocephalus.

as from those delivered vaginally; a further sample was obtained at discharge (eighteenth to twenty-first day post partum).

There was no significant difference between the hemoglobin value at term in the 2 groups of patients. The mean figure for 170 patients was 11.67 grams per 100 millilitres of blood. If the mean figure for normal healthy females is taken as 13.67 grams *per centum*, the figure for women at term is 84.7 per cent of normal. Of the patients delivered vaginally, the lowest mean figure on the third day was 86.5 per cent of the value at term. In the patients delivered by cesarean section, the lowest mean figure on the fifth day was 73.7 per cent of the mean figure at term. The hemoglobin value of the average patient delivered vaginally is, therefore, reduced by 13.5 per cent of its pre-labor value, and that of the average patient delivered by cesarean section is reduced by 26.3 per cent. At discharge from the hospital, the mean hemoglobin value for patients delivered vaginally was 96.4 per cent of the mean figure at term and 82.9 per cent of the mean value for normal females, whereas the corresponding figures on leaving the hospital for patients delivered by cesarean section were 81.7 and 68.8 per cent, respectively. The mean hemoglobin reduction in the 31 patients on whom the classical operation was performed was 22.2 per cent, and in the 30 patients on whom the lower segment operation was performed the mean reduction was 26.2 per cent.

The mean pre-labor plasma protein value for the group delivered by cesarean section was lower than that for the group delivered vaginally. A fall in plasma protein value occurred in both groups, reaching the lowest mean value on the third day post partum. However, by the fifth day the average patient delivered vaginally had recovered the lost protein completely, and at the time of discharge on the eighth to tenth day, she had a higher plasma protein content than at term. At discharge the mean figure was 91.6 per cent of the mean figure for normal females. On the other hand, patients delivered by cesarean section were slower to recover their plasma protein, and at discharge on the eighteenth to twenty-first day, they still had not regained as much protein as those delivered vaginally had regained on the eighth to tenth day. At discharge the mean plasma protein value was 87.6 per cent of the mean figure for normal females.

These findings indicate considerable blood loss in cesarean section, and necessitate consideration of blood transfusion and hematinic therapy in the majority of cases.

## AN EVALUATION OF EXTRAPERITONEAL CESAREAN SECTION

S. A. COSGROVE AND E. G. WATERS

Am. J. Obst. & Gynec., 52: 237-247, 1946

The chief cause of mortality from transperitoneal approach to the pregnant uterus is peritonitis. No expedient involving the broad invasion of the peritoneal cavity is competent in eliminating peritonitis from obstetric practice. In re-

eclampsia. The operation is not employed if the patient appears about to have convulsions. It is occasionally done when the convulsive state has been completely overcome, and it is sometimes necessary when abruption of the placenta occurs, but eclampsia should be one of the rarest indications for cesarean section.

In 213 pregnancies in hypertensive patients carried past 28 weeks, cesarean section was performed in 28 cases with a maternal mortality of 4 per cent and a fetal mortality of 25 per cent. In 185 vaginal deliveries the corresponding rates were 1 and 24 per cent.

Another indication for cesarean section is placenta previa. Of 341 cases, cesarean section was performed in 104, with no deaths. Among the 237 patients delivered vaginally there were 2 deaths.

Classic cesarean section is reserved for those cases in which the uterus is to be removed. There is no valid reason for electing the classic operation in placenta previa, and in the author's opinion, the lower-segment operation is always safer and better. The preference is for low-segment operation with transverse cervical or isthmal incision. It is believed that the Porro operation, as employed in septic cases, is not indicated. In over 500 cases of extraperitoneal cesarean section the mortality rate has been 1 per cent. It is no longer believed that patients die from myometritis, parametritis, or pelvic cellulitis, provided the infected areas are drained, but they still die from peritonitis. In all septic parturient patients, the peritoneal cavity should not be opened. Except for vaginal delivery, extraperitoneal cesarean section is the only way of preventing this. Either the paravesical (Latzko) or the supravescical (Waters) is good, with definite advantages favoring the latter.

## BLOOD LOSS IN CAESAREAN SECTION

LOIS BENSON

M. J. Australia, 1: 842-846, 1946

The present paper reports the results of an investigation designed to compare the hemoglobin value of patients who were delivered *per vaginam* with that of patients who were delivered by cesarean section. This includes the changes in hemoglobin value and plasma protein value of the 2 groups of patients during their stay in the hospital.

One hundred and nine patients, delivered vaginally, were studied. Blood samples were obtained upon admission to the hospital, immediately after delivery, on the third, fourth and fifth days post partum, and just prior to discharge from the hospital (eighth or tenth day). Sixty-one patients on whom cesarean section was performed were studied. The lower segment operation was performed in 30 cases and the classical operation in 31. The indications for section were as follows: disproportion, 40 cases; pre-eclampsia, 8 cases; malpresentation, 7 cases; placenta previa, 3 cases; ruptured uterus, 2 cases; carcinoma of the cervix, one case. Samples of blood were collected from these patients

## SOCIAL AND LEGAL ASPECTS

### THE DEFICIT IN THE BIRTHRATE OF COLLEGE GRADUATES

C. J. GAMBLE

Human Fertil., 2: 41-47, 1946

It has been found, by several investigators, that the number of children born per college graduate to those completing their courses during the last half of the 19th century diminished from decade to decade among the graduates of Harvard College, Michigan State University, Syracuse University, Wesleyan University and Yale College.

Graduates of Harvard of the classes of 1916 to 1920, inclusive, reported an average of 1.73 children per graduate. This is a significant increase from the value of 1.45 found by Phillips for the classes of 1891 to 1900. When the greater survival rate is considered the increase amounts to 26 per cent.

Of the Harvard graduates of 1916 to 1920, 88 per cent were married and of those married, 82 per cent had at least one child. There were 1.97 children per married graduate and 2.38 per fertile marriage.

The class of 1920 at Yale showed similar increase, reporting a slightly greater number of children than the contemporary class at Harvard.

The children born are sufficient to replace only 84 per cent of the 5 Harvard classes studied. The fact that earlier studies found similar results for several colleges suggests that this failure of replacement is generally true of graduates of such institutions in the United States. This should call the attention of the graduates to the threat of extinction and to the impending damage to the nation.

## POPULATION

A. S. PARKE

Lancet, 1: 913-915, 1946

In England and Wales the birth-rate reached its peak of 35 per 1000 in about 1870, after which it fell continuously, so that in 1938 the rate was only 15.1 per 1000. These figures do not accurately convey how the population is replacing itself, for if people begin to live longer, the birth-rate calculated in births per 1000 will automatically fall. The net reproduction-rate is a more satisfactory index, and tells how many female offspring are left by each woman. A net reproduction-rate of 1.0 means that replacement is exact. In 1880 this rate in England, Wales and Scotland was far above 1.0. Since then it has fallen almost continuously; in 1938 it was down to 0.805 in England and Wales.

lation to cases not exhibiting proper conditions for such operations, the authors list several available expedients: (1) delivery of all such cases by vagina, not always safe for mother or child; (2) cesarean-hysterotomy, mutilating, formidable and dangerous; (3) marsupialization and exteriorization of the uterus, appealing so little to good surgical standards as not to rate discussion; (4) exclusion operations, relatively unreliable in efficacy; and (5) extraperitoneal cesarean section, established by the authors' experience as in a high degree safe and efficacious in protecting the parturient against the risk of fatal peritonitis.

The writers propose that all cases subject to cesarean section for feto-pelvic disproportion be divided into the following groups:

#### I. *Clean cases.*—

1. Those not in labor, nor with membranes ruptured, nor subjected to any manipulation, nor showing any intercurrent infection.
2. Those same as above, except with short period of labor, with membranes ruptured not in excess of a minimal time.

#### II. *Potentially infected cases.*—

1. Those in labor more than 24 hours.
2. Those with membranes ruptured more than 12 hours.
3. Those with any other manipulation than very few rectal examinations and/or one ideally guarded vaginal examination.

#### III. *Actually infected cases.*—

All those which, in addition to the factors constituting potential infection, exhibit: (1) exaggeration of those factors, plus (2) actual clinical signs of infection. The worst cases in this group probably constitute what are called the "mismanaged" or "neglected" cases.

In this third group of actually infected cases, the authors prefer to handle the majority of them conservatively, improving the patient's general condition in contemplation of vaginal delivery where possible. When it is necessary to do any suprasymphyseal operation, extraperitoneal section is considered as giving the patient a better chance of survival than transperitoneal cesarean-hysterectomy.

The application of extraperitoneal section to potentially infected cases constitutes its greatest value. Although the percentage incidence of this group of cases is small, it is not yet possible to eliminate entirely such cases from even capable experience.

It is concluded that extraperitoneal cesarean section is an important resource of the obstetric armamentarium in the proper management of all potentially infected or infected cases.

W. J. Dieckmann, as a discussant on this paper, concludes that the infected patient should be delivered vaginally if it can be done without too much trauma, and otherwise, by cesarean-hysterectomy. F. H. Falls discusses the relative safety of the classical cesarean section and the lower segment section. He prefers the lower segment operation because of the lessened mortality.

# MISCELLANEOUS

## THE RELATIONSHIP BETWEEN EPILEPSY AND MATERNAL AGE

G. BEALL AND R. G. STANTON

Human Biol., 18: 49-60, 1946

It appeared that certain characters of some epileptics corresponded to those commonly marking mongolian defectives, suggesting the possibility of a common type of developmental disturbance. Therefore, the authors have studied to see whether the effect of maternal age, at delivery, for epilepsy was similar or opposite to that for mongolism. The present investigation follows the lines of the writers' work on mongolism, being based on a census of the number of patients by age and age of mother, at a given instant, in an institution. Data were obtained from the Ontario Hospitals at Woodstock (for epileptics) and Orillia (for defectives).

TABLE 3  
*Relative epileptic incidences*

AGE OF MOTHER	WOODSTOCK		ORILLIA			TOTAL
	Not defective	Defective	Moron	Imbecile	Idiot	
<i>First calculation</i>						
15-19	1.19	20.93	2.40	12.48	4.97	41.97
20-24	4.27	5.67	3.97	6.06	8.29	28.26
25-29	4.20	4.86	1.59	6.62	7.10	24.37
30-34	3.23	5.87	2.20	8.97	6.61	26.88
35-39	2.72	5.80	2.57	9.97	10.19	31.25
40-44	6.22	6.19	5.38	5.16	3.37	26.32
45-49	15.41	28.88	11.22	11.93	4.85	72.29
<i>On uniform basis of 1.00 for mothers 20-29 years old</i>						
15-19	.28	3.98	.86	1.97	.65	1.59
20-24	1.01	1.08	1.43	.96	1.08	1.07
25-29	.99	.92	.57	1.04	.92	.93
30-34	.76	1.11	.79	1.41	.86	1.02
35-39	.64	1.10	.92	1.57	1.32	1.19
40-44	1.47	1.18	1.94	.81	.44	1.00
45-49	3.64	5.49	4.04	1.88	.63	2.75

These data were calculated by the method devised by Beall and Stanton (1945) which consists of weighting such data by the reciprocal number of women of various ages and by the reciprocal of the birth-rate of women for various ages at the time the patients were born. The point of these calculations is to replace

The increased birth-rate during the war has raised the reproduction-rate to about 0.9. Another effect of war is an increase in the proportion of male children born. In 1942 there were more than 106 males per 100 females, the highest figure ever recorded. It is probably due to earlier marriage, coupled with the increased proportion of males born to young parents.

In spite of the fact that the birth-rate has been falling for 70 years, the population is still increasing. This is explained by the fact that the death-rate has fallen to about one-half what it was in 1871. The expectation of life at birth has increased from 45 to about 65 years. Since there is a tendency toward a greater mortality among males, the excess of males at birth is rapidly dissipated if there is a high infant mortality rate, leaving an excess of females of reproductive age. The falling death-rate has made a remarkable alteration in the age-distribution of population; men over 65 and women over 60 were 6 per cent of the population in 1901, 12 per cent in 1941, and will be 21 per cent in 1971. The economic implications of this change are easily seen.

It is unlikely that the spontaneous wartime increase in the reproduction-rate will be maintained, and to raise the level to 1.0 and keep it there may require positive measures to encourage families. In conclusion, the author considers the quality as well as the quantity of the population, noting that the better stock tends to have smaller families than the careless and irresponsible elements. For those who welcome unlimited state control the solution for this dilemma is control of marriage and propagation. For those who do not favor such interference with the individual, the answer is difficult. 5 figures.

In long labors, the patient should be sustained with carbohydrates in the form of sweetened juices, dextrose intravenously and mild sedation. Dehydration should be avoided, and good mental hygiene established. The Keilland forceps are useful in cases of transverse arrest of the head and occiput posterior positions which are not corrected manually with ease. Pituitrin is very dangerous in long labors. Occasionally an ovarian cyst or small fibroid in the cervix may cause dystocia.

Two valuable diagnostic aids in placenta previa are the x-ray and sterile vaginal examination. The former, in expert hands, can locate the site of placental attachment in 90 per cent of cases. The examiner can find the margin of the placenta by inserting a finger inside the cervix and *gently* sweeping around the entire circumference. In central placenta previa abdominal section is indicated. Marginal varieties in the multipara can be conducted by normal labor, the head acting as a tampon. Transfusion is an important adjunct. Packing, Braxton Hicks version, bags and delivery through an undilated cervix may be harmful procedures. Premature separation of a normally implanted placenta usually calls for abdominal section.

The author discusses also the control of postpartum hemorrhage, the repair of cervical and vaginal lacerations, retained placenta, and mastitis.

numbers of patients by age and age of mother by some quantities so weighted that the cross-totals are independent. On these lines, the data from Woodstock and Orillia were weighted, and totals, by age of mother, found as shown in the first panel of Table 3. A second corresponding panel was formed where the values are so adjusted that the average relative incidence for mothers in their 20's is 1.00; this adjustment facilitates the comparison of the various columns.

There is a general indication in Table 3 that the possibility of epilepsy increases with extremely high maternal age, and possibly with very low. There is also a suggestion that the relation indicated, reminiscent of the situation obtaining for mongolism, is most acute for epileptics of superior intelligence. This study indicates that the probability that a birth will prove that of an epileptic, diagnosed probably idiopathic, is above normal for women in their late 40's. The relation is similar (although more moderate) to that for mongolism. This effect had been anticipated, but not a second difference in the incidence of epilepsy with the intelligence level of the patients.

## MANAGEMENT OF SOME COMMON OBSTETRICAL COMPLICATIONS IN GENERAL PRACTICE

H. L. CHOATE

South. M. J., 39: 585-588, 1946

In this paper the author outlines briefly some procedures which have proved of value in the various complications of an obstetrical practice.

The first complication discussed is the early toxemia characterized by nausea and vomiting. This should be treated vigorously, by psychic measures, sufficient rest, avoidance of sexual relations and a diet which is divided into 6 daily feedings, predominating in carbohydrates, low in fats and moderate in proteins. In the more severe nausea cases dextrose, saline, absolute rest and sedation are indicated.

The early signs of pre-eclampsia (excessive weight gain, edema, rise in blood pressure and albuminuria) should be treated by bed-rest, sedation, limited salt intake and catharsis. Should severe pre-eclampsia ensue and the patient be near term, labor should be induced as soon as the condition permits. Caudal anesthesia is valuable in these cases. In eclampsia, an attempt should be made to control convulsions before inducing labor. The second stage should be shortened by the use of low forceps.

Nephritic toxemia begins earlier and advances more slowly, giving a false sense of security because the blood pressure rises slowly and the patient does not appear very ill. If allowed to progress too far, serious kidney damage may result. Operative deliveries are more indicated in this form of toxemia than in eclampsia.

At 9:30 A.M. she delivered spontaneously of a stillborn premature infant. Her condition immediately began to improve slightly, the blood pressure falling to 130/110 and the pulse improving in quality. At 2 P.M. she was started on 30,000 units of penicillin every three hours and about this time it was noticed that there was a flaccid paralysis of the left arm and leg. There was an absence of the deep reflexes and a positive Babinski on the left. Slight facial paralysis was also noticeable. The urine at this time was found to be grossly bloody. Throughout the next several days her condition remained about the same except that the blood pressure began to rise again. Blood plasma was given in addition to other medications on several occasions. A spinal puncture was requested by one of the consultants and was found to be entirely negative. The patient's condition continued much the same until the morning of January 9. At this time her temperature began to rise rapidly until it reached 105° Fahrenheit by axilla and she went into a state of shock, the blood pressure dropping to 90/60. Her condition rapidly grew worse and in spite of all treatment she died at 8:20 P.M. An autopsy could not be obtained.

*Discussion:* How many years must lapse before every pregnant woman in this country will receive sufficient prenatal care to make deaths from eclampsia a rarity? There is probably no field of preventive medicine which will pay greater dividends in saving the lives of both mothers and infants. The lives of either of these are too great a price to pay for too busy a practice or someone's failure to educate the patient or her husband to the importance of constant supervision during pregnancy. These are often given as alibis for some calamity which is avoidable in many instances. The treatment of a patient with eclamptic convulsions may be as good as the medical world knows how to give today, but too frequently that treatment comes too late. Vigorous and intelligent management of the pre-eclamptic long before the onset of convulsions will yield better results than heroic attempts instituted after the patient has become desperately ill. The early discovery and treatment of remediable conditions and the careful supervision of the mother throughout pregnancy will in most instances result in a healthy mother and baby which, in the ultimate analysis, is the goal toward which everyone entrusted with the care of an expectant mother should strive.

#### CASE NO. 22

The patient was a thirty-eight year old white multipara who was admitted to the hospital on June 1 at 10:30 P.M. She was practically at term and in early labor. Her past history revealed two uncomplicated term pregnancies, the last of which occurred fourteen years ago. The prenatal course at this pregnancy was uneventful and the estimated date of confinement, according to the menstrual history, was on June 12. On admission the membranes were ruptured and the physical examination was negative except for a systolic murmur at the mitral area. Patient's blood pressure was 122/80, temperature 99° Fahrenheit, pulse 84, and respirations 24 per minute. The height of the fundus was 29 cm., fetus was in a R.O.A. position and the fetal heart was heard in the right lower quadrant.

On rectal examination the head was found to be just dipping into the pelvic brim and the cervix was undilated. Labor progressed normally under seconal analgesia which was begun at 12 midnight. At 3:15 A.M. on June 2 the patient was put up sterile and under gas, oxygen and ether anesthesia, she was delivered spontaneously of a full term living child, weighing 6 lbs., 2½ ozs., at 3:30 A.M. following a central episiotomy. One ampule of pitocin was given intramuscularly, a tampon was placed in the vagina and the episiotomy was repaired. At 3:45 A.M. the placenta and membranes were expressed intact. This was followed immediately by a rather profuse bleeding. One ampule of ergotrate was then

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# Maternal Mortality Reports

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*(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.)*

*Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)*

## CASE NO. 21

The patient was a forty year old white multipara who was admitted to the hospital on December 29 at 12:30 P.M. The history on admission was that the patient had been seen by her family physician on the preceding evening. On the morning of admission about 9:30 A.M. she had a convulsion which from its description was clonic in character. Following this the patient became unconscious. A second convulsion occurred in the ambulance while en route to the hospital about 12 noon.

The history obtained from her physician was that he had been caring for her throughout her pregnancy and had been treating her for some sort of kidney involvement for the past several weeks as evidenced by a rather sudden rise in her blood pressure. He had prescribed sodium nitrite by mouth and bed rest for this condition. The husband of the patient stated that she had been complaining of severe headaches for more than a week prior to admission to the hospital and that she had not carried out her physician's instructions to go to bed.

The estimated date of confinement was the early part of March and on admission she was semiconscious and thrashing about considerably. She was of the pyknic type and her blood pressure was 230/120. The head was essentially negative except that there were many teeth missing. The tongue had not been bitten. There was a slight amount of pink stained froth about the mouth. There was no cervical rigidity and the lung fields were clear to auscultation and percussion. The heart was normal in rhythm and force and the pulse rate was 120 per minute. There were no murmurs present and there was no evidence of cardiac enlargement. There was slight cyanosis of the finger and toe nails. The fundus of the uterus measured 20 cm. above the symphysis and the fetus lay in a R.O.A. position. The fetal heart was good. On rectal examination there was no dilatation of the cervix and the presenting part was floating. The rectal temperature was 100° Fahrenheit. The urine on examination showed a four plus albumin.

Immediately upon admission the patient was given  $\frac{1}{4}$  grain of morphine, some paraldehyde and intravenous glucose. The blood pressure dropped quite rapidly so that six hours after admission it had fallen to 135/95. The patient remained unconscious throughout the day. She developed some early signs of pulmonary edema and she was put in an oxygen tent and rapid digitalization was begun. Sedation was repeated several times and more glucose was given at intervals. At midnight on December 30 the patient was catheterized and 250 cc. of dark brown concentrated urine was obtained. The catheter was left in the bladder at this time. By morning the patient's condition was considerably worse. Her temperature was 102° Fahrenheit by rectum, her pulse was thready and too rapid to be counted. The respirations were rapid and labored.

ever, was found to vary from 140/110 to 160/130 and the urine contained a trace of albumin. There was no particular attention paid to this hypertension and the patient was allowed to be up and about in the ward with no special treatment or diet. On February 2 it was recorded that the patient had a slight bronchitis and on February 14 it was recorded on the chart that a slight degree of edema was present. This edema increased so that on February 18 the patient was ordered to bed for a few days. At this time her blood pressure was 150/100. No further attention was given to the patient's supposed bronchitis and no note was made concerning her heart. On February 28 after the patient had been in labor for about twelve hours she suddenly developed severe respiratory distress with an extreme degree of shortness of breath and a great deal of cyanosis. The pulse became imperceptible and the patient showed all the evidences of an acute pulmonary edema. Repeated injections of cardiac stimulants were without result and the patient died undelivered.

No autopsy was obtained.

*Discussion:* There is good probability that this patient had unrecognized cardiac disease. The bronchitis which is mentioned may very well have been a sign of cardiac decompensation. The untreated toxemia and the effects of her labor were sufficient apparently to bring about a state of acute cardiac failure from which she never recovered.

While it is generally agreed that there is a considerable amount of increased strain on the heart during pregnancy and labor, the normal heart satisfies the demands made on it very well. The failure to recognize cardiac disease in a patient by no means proves its absence. The recognition of degenerative processes of the myocardium may well be difficult, and some of the early signs of impending break in compensation at times require the skill of the expert cardiologist to recognize, and he is often not available in many parts of the country.

The association of heart disease with pregnancy is to be greatly feared. Perhaps the greatest advance in this field has been in the more universal use of the New York Heart Association's classification in which patients are grouped and treated depending on the functional capacity of the heart. Important principles in the treatment of pregnant women with heart disease are rest and more rest, and the avoidance of infections. Careful diagnosis, intelligent education of the patient, combined with expert conduct of pregnancy, labor and the puerperium give the patient her best chances for survival when real heart disease complicates pregnancy.

#### CASE NO. 24

The patient was a thirty year old white multipara who was admitted to the hospital during her eighth month of pregnancy for the purpose of inducing labor because she had a premature rupture of the membranes.

On admission on February 6 her temperature, pulse and respirations were normal. One attempt at a medical induction of labor with castor oil, quinine and nasal pituitrin was unsuccessful. On the following day an x-ray of the abdomen was taken which showed a single fetus, apparently weighing between 4 and 5 pounds which appeared to be presenting partially by the vertex with both feet lying near the pelvic inlet and one hand lying beside the head. It was immediately decided to deliver the patient by cesarean section and accordingly a classical section was done on February 7 at which a premature child weighing 4 pounds 11½ ounces was delivered.

The day following the operation the patient's temperature rose 101.3° Fahrenheit and her

given intravenously but by 3:55 A.M. the patient's blood pressure had dropped to 70/40 and the bleeding continued in spite of additional ergotrate and vigorous massage of the uterus. It was immediately decided to remove the uterus and the patient was transferred to the operating room. At 4:10 A.M. 1,000 cc. of 5 per cent glucose was started and at 4:20 A.M. the laparotomy was begun. Morphine grains  $\frac{1}{2}$  and atropine grains  $\frac{1}{16}$  were given at 4:25 A.M. and the introduction of one unit of blood plasma was started. The abdomen was closed at 5:40 A.M. following the hysterectomy. The patient's condition was critical and a second unit of blood plasma was started at this time. At 6 A.M. the patient showed some air hunger and an injection of  $\frac{1}{2}$  grain of morphine was given. There was some bleeding from the vagina and an attempt was made to control this loss of blood with a vaginal pack. All during this time the pulse and blood pressure of the patient could not be obtained and at 6:15 A.M. a blood transfusion was started. The patient's condition rapidly became worse and even though oxygen was administered nasally, respirations ceased at 7 A.M.

*Discussion:* While it is true that in rare instances postpartum hemorrhage may be so profuse that there is little time if any to do very much before the patient is in profound shock, it is nevertheless also a well known fact that the intelligent handling of such cases will save many lives now being needlessly lost. Who has not stopped many a brisk hemorrhage by vigorous uterine massage, using both hands if necessary, one of them inside the uterus and the other on the abdomen? The repair of any extensive lacerations at this point goes without saying. Such treatment in a majority of instances will stop the hemorrhage. The saving of blood is of prime importance, and should the bleeding continue in spite of massage, oxytocics, and the repair of lacerations, the uterus and the vagina should be packed. The firm tamponade of the vagina should always follow the firm packing of the uterus with gauze. In many instances the failure of this procedure is due to faulty technique. The removal of the uterus may in very rare instances be necessary. In many hands this is either done too early or too late.

Not only was a laparotomy done on this patient with insufficient and improper attempts to control the bleeding by other means, but the first blood transfusion was not given until  $2\frac{1}{2}$  hours after she began to bleed freely. In many parts of the country there are innumerable hospitals without either a blood bank of their own or a community bank available. Much that we learned from our war experience about the use of blood has not only failed to penetrate into the smaller cities and rural areas, but alas, has become neglected and ignored in some of the largest cities in the country. The Red Cross organizations have stepped out of the picture and there has been no one in the community sufficiently interested to continue the splendid job which they carried on so well while hostilities were still going on. It seems a pity not to take up where they left off, because many a mother's life is lost in the United States because of the inability to obtain blood quickly and in sufficient quantity.

#### CASE NO. 23

The patient was an eighteen year old colored multipara who was admitted to the hospital on January 22 because it was thought that she was in labor. Her labor pains were quite weak and irregular. On examination her heart and lungs were found to be normal and a diagnosis of a single normal pregnancy was made at this time. The blood pressure, how-

Due to restlessness, paraldehyde was given by rectum. The temperature was 102° Fahrenheit and during the first ten hour stay in the hospital, her urinary output was 550 cc. At 12 midnight, the respirations became very noisy and labored and on examination the heart was found to be grossly enlarged. At 2:15 A.M. there was marked evidence of pulmonary edema and cyanosis, 400 cc. of blood was removed by venesection and rapid digitalization was begun. The patient's course however continued rapidly downhill and she was placed in an oxygen tent and a second venesection was done at 7 A.M. At noon on May 23 she fell into labor and after nine hours delivered spontaneously of a still-born macerated fetus weighing 7 pounds, her condition continued critical and although she seemed somewhat more comfortable following her delivery, evidences of cardiac failure increased and at 4:45 P.M. on May 24 she died.

Postmortem examination was denied.

*Discussion:* The appearance of "eclampsia" on the certificate of death submitted for this patient reveals a very common tendency to diagnose every instance of convulsions and coma in a pregnant patient as eclampsia. In a differential diagnosis we must rule out such things as epilepsy, meningitis, brain tumors, syphilis of the central nervous system, cerebral hemorrhage or thrombosis, uremia, and a host of other conditions. Even hysteria may cause some difficulty unless one is familiar with the true picture of eclampsia.

The classification of the toxemias of pregnancy recommended by the American Committee on Maternal Health in 1937 divides the toxemias into a group of diseases not peculiar to pregnancy and a group of diseases dependent on or peculiar to pregnancy.

This patient falls into the first of these two categories which includes such diseases as hypertensive disease and renal disease. The history is suggestive of cerebral hemorrhage. The complete absence of medical attention until quite late in pregnancy, and the inadequacy of the care even when the patient did finally go to a physician leave little doubt of the preventable nature of this death. Even when one takes into consideration what little facts are known in the cursory history given to us, it is obvious that many elements in the handling of this 45 year old grand multipara would have been different in the hands of a well trained obstetrician if he had been privileged to care for this patient from the very onset of her pregnancy.

#### CASE NO. 26

The patient was a thirty-three year old colored multipara who was admitted to the hospital on June 6 in advanced labor with a transverse presentation and a prolapsed fetal hand. Her family and past history were negative and all of her previous pregnancies had been normal. The prenatal course of the present pregnancy had been normal except for a single elevation of blood pressure of 146/96 which rapidly returned to normal and remained so.

The patient fell into labor on June 6 at 2 A.M. and was seen by her attendant at 2:45 A.M. At this time the presentation was thought to be a vertex and on examination the cervix was undilated. Labor continued until 6:30 A.M. when the membranes ruptured spontaneously. At 8:30 A.M. the right arm and hand prolapsed into the vagina and the patient lost about 200 cc. of bright red blood. She was seen by another physician who made a diagnosis of transverse presentation and advised hospitalization. The patient arrived at the hospital at 10 A.M. at which time she was found to be in mild shock. The pulse rate

pulse rate remained around 130 per minute. The second day after delivery the highest temperature was 101.5° Fahrenheit and the pulse continued rapid. About this time the patient became greatly distended and began to vomit. Treatment with glucose and enemas, Wangenstein drainage and pituitrin did not relieve the distention. On February 10 the highest temperature was 105.4° Fahrenheit, the patient's course went steadily downhill and on the following day she died.

No autopsy was obtained.

*Discussion:* Space does not permit the enumeration of every indication for which the writer has seen a cesarean section performed. It is so often utilized as a way out of a difficult situation by the attendant without adequate obstetrical training, and in some parts of the country is one of the most abused operations performed. Deaths from infection and hemorrhage in association with abdominal delivery play a large role in the total story of maternal mortality. Perhaps we should all go back and read again the century-old writings of Oliver Wendell Holmes and Semmelweis to impress more firmly upon our minds how easily the generative tract may be invaded with microorganisms. Surely the attendant responsible for this patient's death must have heard or read somewhere that it is not considered good obstetrics to do a classical section on a patient with membranes ruptured for several days. Would it be asking too much of our readers to believe that there are still scores of surgeons and even some so-called obstetricians who do a classical section at all times because they have never learned to do the low cervical and extra-peritoneal operations and who pay little attention to established indications for or contraindications to abdominal delivery? Yes, there is still need for better obstetrics in many sections of the country!

#### CASE NO. 25

The patient was a forty-five year old unregistered white multipara with ten living children who was admitted to the hospital on May 22 with an estimated date of confinement some time in June. Because of the patient's critical condition, the only history available was obtained from her husband who stated that so far as he knew there was no history of heart or kidney disease in the patient. He stated that the present pregnancy progressed normally until about the middle of April when the patient began to have considerable shortness of breath, severe headaches and swelling of the ankles. It was then that she consulted a local physician for the first time who told her that her blood pressure was 200/100 and that she should restrict her activities. He did not examine her urine and he prescribed some epsom salts daily.

The patient's symptoms not only continued but gradually grew worse. While working in the fields in the morning of May 22 she had a sudden attack of numbness of the face and the right arm. The lower extremities did not seem to be affected. On the way to the hospital she is said to have had a "spell" of some sort at which time she lost consciousness and "frothed" at the mouth.

On admission the patient was irrational and uncooperative. There was a slight facial weakness evident and the left pupil was larger than the right. On superficial examination there were no other gross neurological changes evident. Her blood pressure was 180/110 and the temperature and pulse rate were normal. During the next seven hours the patient had four generalized convulsions which were noted by observers as typical of eclampsia. On examination she was found to have a full term fetus lying in a R.O.A. position.

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# Gynecology

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## ENDOCRINOLOGY

### INDUCTION OF OVULATION IN WOMEN

#### EDITORIAL

Brit. M. J., 1: 531-532, 1946

Early optimism for inducing ovulation in women faded as it was found that the pituitary-gonad relationship is complicated and delicately balanced. Even today it is difficult, and often impossible, to induce the human ovary to ovulate. The early attempts were made with chorionic gonadotrophin, and failed. Hoffman has concluded that ovulation in lower animals, in primates and in humans depends on (a) follicle-stimulating hormone applied in correct amounts long enough to promote full follicle-ripening; (b) addition of luteinizing gonadotrophin at the moment when the follicle is ripe; and (c) the presence in the ovary of follicular systems capable of responding to these stimuli.

Most workers now use a combination of gonadotrophic principles when trying to induce ovulation in women. E. C. Hamblen copies what appears to be the natural cycle, injecting follicle-stimulating hormone during the first phase of treatment and chorionic gonadotrophin during the second, and he and C. D. Davis have reviewed the results from a 5-year trial of "one-two cyclic gonadotrophic therapy". They conclude that patients who suffer from "hypoestrinism" show a poor response, but that patients with anovular ovarian cycles without "hypoestrinism" respond well; 44.8 per cent of these showed evidence of corpus luteum formation after treatment. However, Hamblen's work will have to be repeated on a much larger scale, and by many independent workers, before it may be claimed that a satisfactory method for inducing ovulation has been found. In contrast to the above results, Geist, Gaines and Salmon have carefully investigated 91 cases after treatment with hypophysial, equine and chorionic gonadotrophins, in various combinations, and failed to find, in any case, evidence of ovulation which could unquestionably be attributed to treatment.

(It is unfortunate, but it is true, that no one has yet been able to devise any method of making non-ovulating women ovulate. The much too premature enthusiasm for equine gonadotrophin, on the basis of the publication of Davis and Koff, has pretty well petered out, as has the employment of the chorionic hormones, or the earlier efforts of the Germans to induce ovulation by jolting the pituitary, so to speak, by means of large "shock" doses

being 136 per minute and of poor volume. Her blood pressure, however, was 124/70. On examination of the abdomen a term pregnancy was palpated lying in a transverse position and percussion well into the left flank revealed marked dullness. While performing a rectal examination about 200 cc. of dark clotted blood escaped from the vagina, the fetal heart could not be heard, the patient was given 500 cc. of 10% glucose and she was typed for transfusion.

Uterine contractions were occurring about every 3 to 4 minutes and the patient was perspiring profusely. One hour after admission the uterine contractions ceased. At this time it was thought that the patient either had a ruptured uterus or a premature separation of the placenta. At 12:15 P.M. the patient suddenly became pulseless, respirations were labored and her condition became critical. She received morphine, more glucose and 500 cc. of whole blood. Her condition improved somewhat for the moment and it was felt that she should have been delivered at this time. Vaginal examination showed a laceration in the lower uterine segment on the left side. A fillet was placed about the prolapsed hand and an internal podalic version and breech extraction was done delivering a stillborn fetus weighing 8 pounds, 13 ounces, at 2:06 P.M. Immediate manual removal of the placenta was done and an examination of the uterus revealed a large rent through which the whole hand could be inserted into the peritoneal cavity. Laparotomy was immediately performed, the patient being given a second 500 cc. of whole blood. The peritoneal cavity contained about 2,000 cc. of blood and a tear in the uterus was found extending from the lower uterine segment well into the body of the uterus. A rapid hysterectomy was performed and while the peritoneal cavity was being closed, respirations ceased.

*Discussion:* Familiarity with the diagnostic methods at our disposal for the determination of the presentation and position of the fetus in utero is expected even of medical students if they hope for a passing grade in Obstetrics. The failure in this case to diagnose the transverse presentation earlier was most important. This error was followed by a series of other mistakes. When the uterus ruptured is not certain, but it probably occurred about 8:30 A.M., when the patient lost her first 200 cc. of blood. Her hospital admission did not take place until an hour and a half later, and at this time she showed some degree of shock, dullness in the flank, no audible fetal heart and more vaginal bleeding. And then more delay. The first blood was not given until more than two hours after admission.

If sufficient damage was not already done, an internal podalic version and breech extraction on almost a nine pound fetus served to complete the tear into the peritoneal cavity and send the patient into such a state of shock that it would have been a miracle had any sort of treatment availed.

pituitary inhibition. The determination of 17-ketosteroids both before and after estrogen administration was abnormally low.

The pathological examination of the excised uterus revealed adenocarcinoma grade 2.

The authors review evidence that in animals estrogenic substance predisposes certain tissues (especially of the breast and uterus) to the development of cancer. Circumstantial evidence indicates that stimulation of the human breast and uterus by estrogens may be one factor in the processes resulting in cancer of these organs. Experimental work on the relationship of estrogens and cancer of the endometrium is less conclusive than in respect to the breast. Although cancer of the cervix has been produced by estrogens, no report of endometrial carcinoma in animals subjected to estrogen treatment has appeared. Estrogens will produce typical endometrial hyperplasia in animals, particularly in the absence of corpora lutea. In man, carcinoma developing on the basis of endometrial hyperplasia has frequently been observed. Novak and Yui, studying endometrial carcinoma in women, found "hyperplasia" in 25 of 104 cases of endometrial cancer. In 21 per cent of patients over 55 years of age hyperplasia coexisted with carcinoma; in only 4.8 per cent of noncancerous women of the same age group was hyperplasia of the endometrium present. Herrell, in agreement with Novak and Yui, states that endometrial carcinoma occurs nearly always in the presence of a persistently proliferative type of endometrium, resulting from the unopposed action of estrogen. Crossen and Hobbs found the late occurrence of menopause about 4 times as high in women with endometrial carcinoma as in a healthy group. Randall reports similar figures.

The evidence cited does not prove, but does strongly suggest, that the unopposed action of estrogens on the breast and endometrium of certain women may result in cancer development. Since the authors have shown by the finding of atrophic vaginal epithelium, after estrogen was withdrawn, that their patient was producing little or no estrogen, the supposition is strong that endometrial carcinoma might not have developed without the administration of extrinsic estrogens. The physician prescribing this hormone to menopausal women should be aware of the possible danger inherent in prolonged treatment without adequate periods of rest. The development of persistent endometrial hyperplasia may be a sufficient reason for the termination of treatment with estrogens.

(Evidence as to the possible incitement of human cancer by estrogenic therapy has been exceedingly scant. It is based chiefly on 2 or 3 cases of breast cancer which have been observed in women who had been receiving such therapy. However, breast carcinoma is so extremely common in women who have received no estrogen, and estrogen therapy has been received by so many thousands who did not develop cancer that certainly the few reports on this subject would not permit definite conclusions.

As the authors of the present paper state, their interesting case likewise is not conclusive, and for the same reason, but I agree with them that it is highly suggestive. As a matter of fact, I have long felt that postmenopausal estrogenic stimulation of the endometrium may play at least a strongly predisposing role in the development of adenocarcinoma, the evidence for this having been presented in the paper by Novak and Yui, to which the authors allude. The postmenopausal estrogen production which has so frequently been noted presumably has its source in the adrenal cortex, and estrogen stimulation or irritation of the

of estrogen given at about ovulation time. Nor can one be enthusiastic about the effects of synergistic mixtures of pituitary sex principles and chorionic gonadotrophins, or the various so-called cyclic plans which have been suggested. The best experimental work in this field has been done by Hisaw and his co-workers, who have apparently been able to fractionate the pituitary sex hormones of the sheep quite satisfactorily. They seem to have established that ovulation is determined by the presence of a considerable amount of the FSH principle and a small amount of the L factor.—Ed.)

## CANCER OF ENDOMETRIUM AND PROLONGED ESTROGEN THERAPY

M. FREMONT-SMITH, J. V. MEIGS, RUTH M. GRAHAM AND HELEN H. GILBERT

J. A. M. A., 131: 805-808, 1946

The authors believe that the case presented in their paper is the first report of endometrial carcinoma in a woman undergoing prolonged treatment with estrogen. They review evidence as to the possible carcinogenic effect on the breast and uterus from prolonged estrogen therapy, and reemphasize the need for caution in the use of this hormone.

The patient, whose case is the subject of this article, was admitted to the hospital in 1919, at the age of 25, with severe asthma. She has been under almost constant observation for the past 18 years. Pelvic examinations in 1919, 1924, 1942 and 1943 were negative. In 1928 and 1936 she suffered from periods of amenorrhea, and in 1937 a relationship between amenorrhea and the increased severity of her asthma was suspected. The patient, now 43 years of age, complained also of hot flashes and sweats. Estrogenic treatment was begun May 10, 1937, and was given almost continuously until September 22, 1945. During this therapy 3 unusual features were noted: the persistence of hot flashes; the persistence of high urine titers of the follicle stimulating hormone in spite of adequate estrogen dosage; and the absence of bleeding when estrogen was temporarily withdrawn. In January, 1942, an endometrial biopsy showed hyperplasia of the endometrium, but the estrogen was continued. During 1944 vaginal staining occurred. In September, 1945, the patient reported 6 weeks of slight vaginal bleeding. A vaginal smear was positive for endometrial cancer, and the diagnosis of endometrial adenocarcinoma was established from examination of curettage material.

Because of the previous absence of response of the follicle stimulating hormone to prolonged estrogen administration, an experiment was conducted to determine if this same unresponsiveness to estrogens was still present. Estrogens were omitted for a 4-week period, at the end of which the vaginal smear showed complete absence of intrinsic estrogenic stimulation, and the urine titer of the follicle stimulating hormone was high. The administration of estradiol dipropionate, 5 mg. every other day for 10 days, was followed by moderate

(1) disturbance of the autonomic nervous system, such as flushes, sweats, irritability, nervousness and sleeplessness; (2) local genital atrophies, resulting from failure of production of estrogenic hormone; (3) disturbance in the other glands of internal secretion, such as hyperthyroidism, diabetes and metabolic disturbances; and (4) disturbances in the other organ systems, such as nervous, cardiac, renal, hepatic, etc. The menopausal symptoms extend beyond the local genital sphere; therefore, a very complete physical examination should precede attempts at therapy. One may assume that the menopausal symptoms are brought about by the combination of absence of estrogen in the presence of large quantities of follicle-stimulating hormone. Against this hypothesis are the following factors: (1) many women have menopausal symptoms long before the cessation of menstruation and in association with relatively normal hormonal findings; (2) the administration of large doses of follicle-stimulating hormone in cases where estrogen is absent from the urine evokes no menopausal symptoms; and (3) the administration of follicle-stimulating hormone during the menopause does not increase menopausal symptoms, nor does it help symptomatically. Thus, we have no precise explanation of the exact mechanism for the production of symptoms.

The number of hot flushes or sweats per day may serve as an index for therapy. A patient with 30 or more flushes a day is given 50,000 I.U. of estrogenic hormone twice a week by intramuscular injection, this treatment being maintained for about 4 weeks. When symptoms are alleviated the frequency of injections is diminished, and eventually the dosage is decreased and given by mouth until an effective minimal dose is reached. In addition, calcium is administered to diminish the irritability of the autonomic nervous system.

The author does not believe that the good results obtained by the use of estrogens are due solely to their psychic effect on the patient, nor does he agree with the contention that estrogen administration for menopausal symptoms merely postpones the inevitable symptoms to a later date. Also, he does not believe that the estrogens produce carcinoma in the human. However, he feels that the estrogens are contraindicated in patients who have, or have had, malignant lesions of the breast or genital tract. They are also contraindicated in patients who have been radiated for excessive uterine bleeding.

(The author's discussion of the endocrine mechanism of the menopause is sound, though there will be differences of opinion on one or two of his observations on therapy. Contrary to his statement that many women have menopausal symptoms while still menstruating normally, my own observation has been that this is at least relatively uncommon, and that under such conditions, any vasomotor symptoms which may be noted are mild and usually call for no organotherapy. As a matter of fact, one of the many abuses of estrogenic therapy is to resort to it if a woman over 40 develops various nervous symptoms wrongly interpreted as menopausal, even though the woman's ovaries are still functioning quite normally, and probably producing adequate amounts of estrogen. With this statement I feel sure that the author, who is a leading endocrinologist, will agree.

My own feeling is that estrogenic therapy should be employed only in the presence of typical vasomotor symptoms, and only when and if such symptoms are sufficiently troublesome to constitute a real problem. If they are mild and easily borne, the woman is better off

endometrium, unopposed by what many believe to be the protective influence of progesterone, may lead to actual cancer. There is other evidence along this line, some of which has been adduced by the authors.

On the other hand, there is another angle of this question which is worth mentioning. I refer to the fact that the ill-advised use of estrogen may lead to postmenopausal bleeding, that endometrial hyperplasia may be produced, but that this hyperplasia may be of a very proliferative adenomatous type instead of the common and very frankly benign Swiss-cheese variety. This proliferative type of hyperplasia may histologically simulate carcinoma, and I know of several instances in which such errors of diagnosis have been made. This comment is not intended to apply to the authors' case report, for they are well-trained pathologists whose microscopic diagnosis will not be questioned.

However, to illustrate how mistakes can occur, I may cite an experience of my own. Some years ago I received a long-distance call from the president of a prominent drug manufacturing firm, who was rather perturbed because the curettings from a woman suffering from postmenopausal bleeding following stilbestrol therapy had been diagnosed as adenocarcinoma in a mid-western laboratory of pathology. I was asked to examine the slides, which I interpreted as a highly proliferative but benign hyperplasia. I advised repeating the curettage in a month or so, the stilbestrol therapy of course having already been discontinued. The second slide showed a strikingly different picture, the endometrium having reverted to a typical senile atrophic pattern, with not the slightest suggestion of malignancy.—Ed.)

## THE MENOPAUSE, AND ENDOCRINE DYSFUNCTION

R. KURZROK

Hebrew M. J., 1: 192-202, 1946

The author discusses the problem of the menopause, its symptomatology and treatment. He concludes that, while much has been learned in recent years concerning the mechanism and therapy of the menopause, there is need for a still greater amount of knowledge for the understanding of the intricacies of the problem.

Three potential explanations for the etiology of the menopausal syndrome are: (1) failure of the anterior pituitary gland; (2) failure of the individual to respond to ovarian hormones; and (3) inherent failure of the ovary proper. The theory that the menopause is due to failure of production of pituitary gonadotropin is not acceptable, since during the menopause and for some years beyond it there can be demonstrated an excess of pituitary gonadotropins in the blood and urine. In spite of this the ovary does not function. In answer to the second theory, it is well known that the administration of estrogenic hormone in proper dosage alleviates menopausal symptoms, which means that the body tissues respond to stimulation. As regards the third theory, results of experiments by the author have shown that to a given dose of gonadotropins, the ovary becomes less responsive with age. Therefore, it is felt that the etiology of spontaneous menopause is due to the failure of the end organ, namely the ovary, to respond to pituitary stimulation.

In general, the symptoms of the menopause may be grouped into 4 categories:

usually stop such bleeding 4-5 days later. Diagnostic curettage is indicated if the bleeding does not respond. The second type of uterine bleeding due to estrogenic therapy is that associated with continued use of estrogen; this is associated with a benign hyperplasia of the *endometrium*. Such bleeding usually responds well to diminished dosage or discontinuance. The risk of bleeding is greater with stilbestrol than with the natural estrogens. Maintenance dosage over indefinite periods of time is to be condemned; there is some reason to believe that prolonged treatment may even extend the duration of menopause. Margolese has treated cases with menopausal syndrome with combined estrogen-androgen therapy to eliminate masculinization with androgens alone, and bleeding with estrogens alone. The author concludes that since uterine bleeding in the postmenopausal years brings up the possibility of cancer, and is evidence of overtreatment, the trend is toward smaller dosage, less than 0.5 mgm. stilbestrol daily in nearly all cases, and shorter duration of treatment (weeks rather than months).

Realizing the disagreeable nature of the side effects, and the possibility of underlying tissue damage, the estrogen should be kept at minimum effective dosage. The mode of administration should be selected for best over-all results. It must be remembered that the menopause is a self-limited phenomenon.

(This is an excellent paper, crystallizing nicely the hazards of estrogen therapy. While there is little or no evidence that estrogen has actually caused any case of human cancer, there are certain experimental and clinical observations which make us feel that it may be at least a predisposing factor in some cases. Some of these have been discussed by the author in his paper. It does seem true that women with late menopause show a higher incidence of later adenocarcinoma of the uterus than those who have the menopause at the usual age. Again, the recently published study of Corscaden indicates that women who have had functional menopausal bleeding are about  $3\frac{1}{2}$  times as likely to develop later adenocarcinoma as others. Finally, I am more and more convinced that there is some relationship between postmenopausal hyperplasia, which is an estrogen-induced lesion, and adenocarcinoma, as was stressed in our paper on the subject in 1936 (Novak and Yui, *Amer. J. Obst. & Gynec.*, 32: 674, 1936).

Conceding all these possibilities, there appears to be no reason for depriving the menopausal woman of properly conservative estrogen therapy in the minority of cases in which this is indicated. However, one should be very circumspect, in the present state of the question, in women who harbor a so-called precancerous lesion of any sort, or in those who present a family history heavily laden with cancer. In the occasional case of this sort, the clinician will choose to employ testosterone instead of estrogen, as it, like the latter, is effective in the relief of vasomotor symptoms. See also comment on preceding abstract. —Ed.)

## THE FEMALE SEX HORMONES

P. M. F. BISHOP

Practitioner, 156: 465-467, 1946

The author presents a brief review of the production of the female sex hormones and an outline of their clinical uses.

not to be started on a career of estrogen therapy, and simple reassurance and explanation may be all she needs. For such reasons as I have mentioned I am also opposed to stereotyped plans of one sort or another, recommending so many thousand units of this or that preparation on regular schedule, often without any admonition to the patient as to time limitation of such treatment, which can do harm if too prolonged. I am one of those who believe that the duration of the menopause can actually be prolonged by indiscriminate and too prolonged estrogen therapy, not to speak of the hazard of inciting postmenopausal bleeding, which may worry both patient and physician.

Finally, to air my personal tenets still more, I see little need for hypodermic medication, with its very real hazard of creating "shot" addicts, now that we know the effectiveness and convenience, not to speak of the cheapness, of oral estrogens, especially those of non-hormonal nature (diethyl-stilbestrol, hexestrol, premarin, benzestrol, ethinyl estradiol, etc.). I myself now rarely use hypodermic organotherapy in menopausal cases. There are some who believe that the natural estrogens give the patients a sense of "well-being" not conferred by the non-hormonal estrogens, but I have not been able to convince myself of the correctness of this observation.—Ed.)

## DANGERS IN ESTROGEN THERAPY; WITH SPECIAL REFERENCE TO SYNTHETIC ESTROGENS IN MENOPAUSAL THERAPY

J. P. SATTERWHITE

J. Bowman Gray School Med., 4: 76-80, 1946

The author discusses the dangers of estrogen therapy under 3 headings: (1) estrogens and neoplastic disease; (2) estrogens and uterine bleeding; and (3) toxicity of the estrogens.

There is little doubt that continuous and excessive estrogenic treatment will result in changes indicative of tissue damage in the organs in which tumors arise. There have been no conclusive demonstrations of the relationship of estrogens to the etiology of human cancer, with the exception of one possible case. However, estrogenic stimulation has definitely produced endometrial hyperplasia and squamous cell hyperplasia, enlargement of cervical glands, cervical erosion and eosinophilic adenoma of the anterior pituitary in the human female. Crossen and Loeb found that 60 per cent of women with uterine cancer continued to menstruate after the age of 50 years, while among a large number of women not affected with uterine cancer, only 15 per cent were menstruating at this age. The possibility of a relationship between estrogens and cancer development is strong enough that estrogenic therapy should be prescribed only where clearly indicated and after complete physical examination, and no patient with past cancer or family history of cancer should receive indiscriminate therapy. Preferably, estrogen should be administered only in those cases which can be controlled and followed.

Estrogens may produce uterine bleeding of 2 types. The first type is true withdrawal bleeding, due to a drop in the estrogen level after withdrawal of the drug. This usually occurs after sudden withdrawal of relatively large doses of estrogens. Progesterone 2-5 mgm. daily for 5 days at the end of treatment will

only 13 patients. Of these 13 cases, 3, who were apparently stable colored women, were told purposely that they must take female sex hormones after they went home. All 3 have insisted on continuing this treatment in spite of the fact that it was originally only suggestive therapy.

The author believes that, following operative procedures involving the female sex organs, there is a definite psychic reaction. These women have been told by a neighbor, friend or mother that once they have their female organs removed they will become fat, lazy, disinterested and develop a negative libido. If they are doubtful of this, their doctor will remove the doubt when he prescribes sex hormones. Over 2200 women have been admitted to the neuropsychiatry service during the past 3 years, and over 1670 of these women have received estrogenic hormones.

When estrogens were first given for so-called menopausal symptoms, the doses were surprisingly low: 10-15 units. In spite of such ineffective dosage, excellent results were reported. The fact that, more recently, the same results have been obtained with placebo therapy and inadequate dosage as with potent doses of estrogen suggests that such results are obtained on the basis of psychotherapy. However, this is a poor type of psychotherapy, since it tends to cause the patient to attribute all of her symptoms to her sex organs, focusing her mind on those organs, and to build up an imaginary chain of symptoms "which makes it difficult for even the well-trained conservative operator to refrain from a laparotomy."

The work of Zondek on male mice, the appearance of breast cancer in women after the use of estrogens, and the rapid development of cervical cancer in women who have leukoplakia make this drug, if nothing more, most interesting as possibly containing a carcinogenic factor.

The author uses estrogen for juvenile gonococcal vulvovaginitis, senile endometriovaginitis, uterine hypoplasia, cramping uterine dysmenorrhea (tentatively), postpartum breast engorgement, some types of habitual abortion, and its effect on ovulation. However, it is believed that estrogenic therapy, as used today, is too often only a psychotherapeutic agent.

(This paper strikes a definitely reactionary note. Weaver's attitude toward estrogenic therapy, especially in menopausal cases, is exactly like that expressed by many gynecologists in the days before the ovarian hormones were isolated and made available clinically. In those days ovarian therapy meant the administration of whole ovarian substance, ovarian residue or corpus luteum. Those who were skeptical of any virtue in such therapy, explaining any good results by their psychotherapeutic value alone, are now known to have been right, for the preparations then available we know now were almost completely inert. And yet many excellent clinicians honestly thought them to be effective in the treatment of menopausal symptoms. The late Dr. William P. Graves, one of the country's leading gynecologists, made the statement that he looked upon corpus luteum therapy as practically a specific for this indication, although the preparations he employed have been shown to contain little or no ovarian hormone.

However, the last 25 years have seen notable advances in endocrinology and biochemistry, and we now have available ovarian preparations of unquestioned potency, even in the cold light of laboratory investigation, which could never be said of the ovarian preparations of an early day. To say that psychotherapy plays no part in the generally satisfactory present day management of the menopause would be absurd. This applies with especial

The chief clinical uses of the follicular hormone are: (1) to relieve menopausal symptoms; (2) to induce uterine hemorrhage in cases of amenorrhea; (3) to relieve pain in certain selected cases of spasmodic dysmenorrhea; (4) to prevent postpartum breast engorgement when breast-feeding is contraindicated; and (5) to allay symptoms and delay progress of prostatic carcinoma. Estradiol is the true follicular hormone, and is administered as injections of estradiol benzoate in doses of 10,000 to 50,000 I.B.U. Five injections, twice weekly, may induce bleeding in cases of amenorrhea. Estrone, a derivative found in pregnancy urine, given orally in doses of 3,000 or 6,000 I.U. will generally relieve menopausal symptoms. The synthetic estrogens are much cheaper and more potent, especially by oral administration, than the natural estrogens. However, they are more liable to induce toxic effects. Stilbestrol is given daily by mouth in fortnightly courses of one, 2 or even 5 mg. for amenorrhea or dysmenorrhea. For breast engorgement it may be given in doses of 5 to 15 mg. daily. In menopausal cases dosage should not exceed one mgm. daily, and symptoms may be controlled with 0.1 to 0.25 mgm. daily. It is important not to use the higher doses in women of child-bearing age for longer than 3 weeks at a time.

For excessive and irregular menstrual bleeding 4 injections of 10 to 20 mg. of progesterone are given every other day in the premenstrual week or on the first day of bleeding. For habitual abortion 5 mgm. of progesterone every other day are injected up to the fourth month of pregnancy.

Up to the present time, the results of gonadotrophic therapy have been disappointing. Theoretically these hormones stimulate the ovary to produce estrogen and progesterone and are therefore employed in cases of ovarian failure associated with menstrual disorders, such as amenorrhea and menorrhagia. Chorionic gonadotrophin is ineffective in these conditions when given alone, and it is usual to give 5 injections of serum gonadotrophin, followed by 3 or 4 injections of chorionic gonadotrophin. The former is usually given in double the dose of the latter; i.e., 200 to 3,000 I.U. and 100 to 1,500 I.U., respectively.

(This is a very sensibly conservative paper by one of the leading gynecological endocrinologists of Great Britain. The dosages recommended by him serve to indicate average cases, though stress may again be laid upon the importance of adapting the dosage and the duration of therapy to the indications of the individual case, as discussed more fully in the comments on the two preceding abstracts of papers by Kurzrok and Satterwhite.—Ed.)

## ESTROGENIC HORMONES, OFTEN ONLY A PSYCHOTHERAPEUTIC AGENT

JOHN D. WEAVER

South. M. J., 39: 581-585, 1946

During a period of 34 months 209 bilateral oophorectomies have been performed at the author's clinic. Estrogenic hormones have been given postoperatively to

gens and estrogens were given simultaneously to 2 castrate opossums and similar dosage controls for each hormone were given alone to 6 castrate animals. There was no antagonism between the 2 hormones. With a few exceptions they were additive in their effects on the tissues of the accessory organs.

It was apparent that both the lack of antagonism between the sex hormones and their inherent bisexual property, previously demonstrated in pouch-young and juvenile stages, are maintained in the adult period.

Intracellular glycogen was observed following treatment with estrogen, androgen and PMSG preparation (only traces with the latter hormone) in the stratified squamous epithelium of the lateral vaginal canals and urogenital sinus, in the prickle and transitional cell zones, but not in the basal zone, cornified cells or in fresh "vaginal" smears tested by iodine vapor. The "vaginal" pH showed no significant change following hormonal treatments. 5 plates.

(In spite of the striking species differences in the effects of most of the hormones, it is of interest to note that, in so far as the equine and human chorionic gonadotrophins are concerned, the results observed by Morgan in the opossum are not unlike those noted by most investigators in the human ovary, i.e., the production of cystic follicles with usually an absence of luteinization.—Ed.)

force to the improper employment of estrogens for a whole array of symptoms, chiefly nervous or psychic, which often occur in the fifth decade, but which are not menopausal at all. If estrogens give good results in such cases, it is reasonably certain that this is by way of the psychic route alone.

But the clearly menopausal vasomotor symptoms are definitely objective. The flushes and sweats can be seen and counted, and their frequency can be strikingly lessened by estrogen therapy. It is true that psychic factors may increase the severity of these vasomotor disturbances, but they may occur in the most tranquil and phlegmatic of women. The fact remains that estrogen therapy, when properly employed in the small minority of menopausal women in whom the vasomotor symptoms constitute a real problem, has established itself as both rational and effective. Even the hard-boiled skeptics of the early joy-riding days of indiscriminate ductless gland therapy have been convinced. I personally do not know of any gynecologist who does not employ estrogens for the indication under discussion. Some undoubtedly use such preparations too indiscriminately, and I have on various former occasions commented upon some of the common abuses, and also upon the supposed danger of inciting cancer growth.—Ed.)

## SEXUAL RHYTHMS IN THE REPRODUCTIVE TRACT OF THE ADULT FEMALE OPOSSUM AND EFFECTS OF HORMONAL TREATMENTS

C. F. MORGAN

*Am. J. Anat.*, 78: 411-463, 1946

In this study it was found that the reproductive tract of the female opossum underwent a seasonal rhythm; the height of sexual activity occurred during the breeding season (February to July); reproduction did not take place during anestrus. A secondary rhythm existed within the breeding season during polyestrus cycles.

Gonadotropins from pregnant mare serum (PMSG) and from human chorionic gonadotropin (HCG) were administered alone and in combination by subcutaneous injections to 17 adult females in anestrus in order to discover the effects of the natural ovarian secretions on the accessory reproductive organs. Responses were elicited from the atrophic ovaries and reproductive tract. The responses of the ovaries to PMSG were production of large cystic follicles and a total absence of luteal cells except for scattered luteinization following the highest dosages. Luteal cells were found following the combination of PMSG and HCG and with HCG alone.

Estrogens were administered to 14 adult females of which 8 were castrated prior to treatment. The results were similar in both castrate and intact animals; the structure of the reproductive tract was like that of the proliferative period of the estrus cycle and following PMSG administration.

Androgenic treatment was given to 12 adult opossums in anestrus, 8 of which were castrated prior to treatment. Responses in the atrophic reproductive tract of the intact and castrate animals were similar and apparently duplicated in many respects the results following PMSG and estrogen administration. Andro-

gens and estrogens were given simultaneously to 2 castrate opossums and similar dosage controls for each hormone were given alone to 6 castrate animals. There was no antagonism between the 2 hormones. With a few exceptions they were additive in their effects on the tissues of the accessory organs.

It was apparent that both the lack of antagonism between the sex hormones and their inherent bisexual property, previously demonstrated in pouch-young and juvenile stages, are maintained in the adult period.

Intracellular glycogen was observed following treatment with estrogen, androgen and PMSG preparation (only traces with the latter hormone) in the stratified squamous epithelium of the lateral vaginal canals and urogenital sinus, in the prickle and transitional cell zones, but not in the basal zone, cornified cells or in fresh "vaginal" smears tested by iodine vapor. The "vaginal" pH showed no significant change following hormonal treatments. 5 plates.

(In spite of the striking species differences in the effects of most of the hormones, it is of interest to note that, in so far as the equine and human chorionic gonadotrophins are concerned, the results observed by Morgan in the opossum are not unlike those noted by most investigators in the human ovary, i.e., the production of cystic follicles with usually an absence of luteinization.—Ed.)

## THE MENSTRUAL CYCLE

### THE TREATMENT OF DYSMENORRHEA

A. BOURNE

Practitioner, 156: 464-465, 1946

In considering the treatment of dysmenorrhea, it is important to recognize the personality type of the patient and the type of dysmenorrhea. In this article the author deals with the sharply defined group of patients that suffers severe, often prostrating pain for a few hours immediately after the flow is noticed. Treatment includes drugs, hormones and operations. No amount of so-called "hygiene" will improve the condition of true spasmodic dysmenorrhea.

In adolescents anodynes may be used but they will soon cease to have effect. Pethidine is a useful analgesic for less severe cases, but it usually causes a "doped" sensation which may last for some hours. Belladonna is sometimes of real value, and may be given as 10 minims of the tincture, or as atropine,  $\frac{1}{100}$  grain, in half an ounce of water.

On the assumption that the ovarian hormone secretion needs reinforcing, a scheme of treatment may be given as follows: During the week after the period—dienestrol, 0.3 mgm. daily for 7 days; during the week before the period—antuitrin-S, 200 units, by injection on alternate days, and dienestrol, 0.1 mg. daily. When the menstrual flow is above the normal it is well to omit all dienestrol and give antuitrin-S alone during the premenstrual week. Thyroid extract should be administered to abnormally fat patients. In thin subjects, with marked weight gain immediately before the period (indicating water retention due to a high level of secreted estrogen), all "estrols" should be eliminated and large doses of antuitrin-S given during the premenstrual week. All hormone treatment is based upon flimsy evidence, and is still largely empirical.

In cases where drugs and hormones fail, the usual procedure is cervical dilatation; however, this too is empirical. There are a number of successes following dilatation in nulliparae. Sympathectomy of the hypogastric plexus should seldom be considered before the age of 30, since it is followed by uncertain results. It undoubtedly has cured some severe resistant cases. Hysterectomy may be necessary during the later years for intractable pain which results in economic loss, risks the resort to morphine, or leads to secondary neurosis.

(In 1915, before the days of over-enthusiastic endocrine therapy for dysmenorrhea, I wrote a paper on the atropin treatment of dysmenorrhea, reporting good results in many cases. In these days of waning enthusiasm for endocrine treatment of dysmenorrhea, it is well to remember the premenstrual administration of atropin as one of the measures which may be employed, because it is certainly helpful in not a few cases. I was interested to read that Bourne also makes use of this drug and finds it of value. While large doses of estrogen in the preovulatory phase often are helpful, at least for one cycle, in making the next period painless through the inhibition of ovulation, there would seem to be no logic

or advantage in combining this plan with the premenstrual use of antuitrin-S, involving as it does a whole lot of undesirable hypodermic treatment. Sympathectomy should not be done if simpler measures make the patient reasonably comfortable, but it is certainly preferable to hysterectomy. The general experience with it indicates that it gives satisfactory pain relief in approximately 70 per cent of cases.—Ed.)

## THE STEM PESSARY FOR DYSMENORRHEA

J. C. POTTER

New York State J. Med., 46: 1346-1347, 1946

The author concludes that a glass stem pessary helps the patient with dysmenorrhea, but does not cure her. In addition, some medication should be given with menstruation. These conclusions are drawn from the study of 25 patients with dysmenorrhea severe enough to necessitate their losing from one to 7 days with each period. Five patients had vomiting as a symptom. Prior to the insertion of a pessary, standard treatment was administered, including sedatives, antispasmodics, rest, exercise and good food. All patients were given thyroid medication and most also progesterone products. When these measures proved of insufficient value, the cervix was dilated under anesthesia and a glass stem pessary was inserted and sutured with mattress sutures of silkworm gut. Of the 25 cases, none were cured, none were made worse, 3 were not helped and 22 were helped. By "helped" is meant that these patients, with medication, could keep at work, rely on completing plans and be on their feet during menstruation. The author believes that it should be emphasized that the therapeutic value of a stem pessary in patients with dysmenorrhea is that it helps, not cures, such patients.

(The stem pessary treatment of dysmenorrhea appears to have been abandoned except in a few clinics. The supposed rationale for its employment was that it kept open a canal whose angulation and narrowness were at one time thought to be the cause of the dysmenorrhea, although this concept has long since then been disproved. Others urged that the pessary, acting as a foreign body, stimulated uterine contractions, thus exercising and developing the uterine muscle. This supposedly corrected the hypoplasia which some thought to be the important causative factor in the pain, though this idea likewise is no longer accepted.)

The good results reported by some in past years have been about as hard to evaluate as are the results of most other treatments of dysmenorrhea, because of the difficulty of eliminating the psychic factor. But the bad results which were reported from time to time were very objective. Aside from even grave pelvic infection in the occasional case, there is no doubt that the retention of a stem pessary in the cervical canal for often a good many weeks is often followed by a troublesome and persistent cervicitis. The treatment of primary dysmenorrhea is still far from satisfactory, but some improvement has occurred. There are a sufficient number of other and safer plans at our disposal without impelling most of us to go back to the stem pessary, which, in spite of the claims of its few remaining adherents, can not be considered free of hazard.—Ed.)

THE ROLE OF THE THECA CELL IN IRREGULARITIES OF THE  
BABOON MENSTRUAL CYCLE

A. CULNER

South African J. M. Sc., 11: 55-69, 1946

Follicular growth, atresia, corpus luteum formation and menstruation in the baboon are similar to those which occur in man. Turgescence and deturgescence of the perineal sex skin during each cycle provides reliable indications of events within the ovary.

The cells of the theca interna have been shown to undergo slight or no change in relation to primordial, maturing, atretic and cystic follicles in the presence of normal ovarian and uterine function.

The theca cells may undergo lutein changes not only in association with a corpus luteum, but also with atretic and cystic follicles. They may give rise to theca lutein cysts and yellow bodies which resemble corpus luteum cysts and corpora lutea, respectively. Although examination of serial sections of these tissues is most helpful, it may not resolve the difficulties in diagnosis. When these lutein changes are sufficiently extensive and numerous, the ovary macroscopically presents numerous discrete or several confluent yellow or pale yellow patches, varying from the size of a pin point to that of a pea, related to atretic or cystic follicles. Microscopically, they are similar to the interstitial bodies described in primates and lower forms.

Yellow bodies of theca cells may be classified according to the extent of thecal involvement and in relation to stages of follicular atresia and cyst formation.

The relation of the theca cells to irregularities of the menstrual cycle and to abnormalities of the endometrial pattern are shown. Reference is made to the progestogenic, androgenic and estrogenic properties of theca cells. Although no specific hormone can as yet be attributed to them, their hormonal activity was influenced by defined factors governing endocrine function. Thus, the hormone of theca cells, whether androgen, estrogen, progesterone or a combination of these, may produce the abnormal manifestations in the menstrual cycle which are found coincidentally with yellow bodies of theca cells. 11 figures.

(Much of what the author states as to theca cell luteinization in the baboon's ovary applies also to that of the human female. Certainly such luteinization is often conspicuous in the corpus luteum of menstruation, and even more in that of pregnancy, though its exact endocrine significance is not known. Lesser degrees of luteinization are often seen in the thecal cells of atretic follicles, the curious thing being that in one and the same ovary some atretic follicles show marked thecal change and others none at all, even though they appear to be of about the same size and the same retrogressive phase.—Ed.)

## VULVA AND VAGINA

### PREVENTION AND TREATMENT OF CARCINOMA OF THE VULVA

B. P. WATSON AND S. B. GUSBERG

*Am. J. Obst. & Gynec.*, 52: 179-190, 1946

This study is based on a series of 30 cases of carcinoma of the vulva, in 25 of which the lesion was definitely primary on the vulva. The authors emphasize that vulvar conditions which are related to the development of cancer are seen with some frequency, and that any irritated or ulcerated lesion which does not yield within a very short time to simple therapy should be subjected to biopsy by free excision. Because of the direct relationship between leukoplakia of the vulva and cancer, every leukoplakic area which causes constant itching necessitating scratching—with consequent breaking or fissuring—should be excised. In such cases, ointments, hormones and x-ray therapy are not justified. Important symptoms in the present series were pruritus in 16 cases, a lump in 18 cases, pain in 6 cases and local discharge in 2 cases. The average delay between the onset of symptoms and treatment of the cancer was  $3\frac{3}{4}$  years. Pruritus is a particularly significant symptom in middle-aged women, and its importance cannot be overstressed.

The average age of these patients when first seen was 59 years, indicating the high incidence of the disease in advanced years. Seven patients were 70 years of age or over, and 11 patients 65 years or more. The youngest patient was 37 years of age; thus, the general age incidence figures should not be permitted to influence the differential diagnosis in the individual with a vulvar lesion.

The survival rates for the patients in this series were 56.6 per cent at 2 years after treatment, 50.0 per cent at 3 years after treatment and 36.6 per cent at 5 years after treatment. The group was treated by various methods which are shown in Table III.

The treatment employed is primarily surgical. The authors have discarded radiation as a primary treatment, except as a palliative. It is important to note that none of the patients treated by simple partial vulvectomy has died with the disease. The authors believe that excision of this type is the best biopsy method for vulvar lesions, and that it will save cases where the malignancy is low grade from unnecessary radical operation. Wide local excision is considered an adequate treatment for basal cell lesions and for squamous-cell lesions of borderline or potential malignancy.

In the usual case with carcinoma of the vulva, the authors prefer complete vulvectomy with bilateral groin dissection. Their technique is a one-stage operation which dissects the superficial inguinofemoral nodes bilaterally, and completely removes the vulvar structures.

Examination of the fatal cases reveals the gravity of prognosis with extension of the disease into the vagina. Only one patient died with the disease more than 2 years after treatment, and the lesion from which she died was a new carcinoma rather than a recurrence. Only one patient with a lesion confined to the vulva and with complete operation performed died of recurrence. 3 figures.

(There will be general agreement with the prophylactic admonitions of the authors, viz., the importance of removal of intractable irritative lesions, especially leukoplakia, and the ineffectiveness of hormones and x-ray therapy in the treatment of such lesions. More puzzling, however, is the discussion of the authors as to the surgical treatment of vulvar carcinoma, especially in view of the recent trend toward an operative plan more radical than that represented by vulvectomy plus bilateral inguinal adenectomy. Taussig's studies, more than any other factor, are responsible for the growing preference for the Basset type of radical operation, when the general condition of the patient warrants this plan, and

TABLE III

*Treatment*

PRIMARY TREATMENT	NO. OF CASES	DEAD WITH DISEASE
Complete vulvectomy with bilateral groin dissection . . .	5	1
Above surgery plus radiation . . . . .	2	1
Complete vulvectomy with unilateral groin dissection . .	2	0
Above surgery plus radiation . . . . .	1	0
Complete vulvectomy . . . . .	2	0
Above surgery plus radiation . . . . .	1	1
Partial vulvectomy with bilateral groin dissection . . . .	1	0
Above surgery plus radiation . . . . .	0	0
Partial vulvectomy with unilateral groin dissection . . .	0	0
Above surgery plus radiation . . . . .	1	0
Partial vulvectomy . . . . .	8	0
Above surgery plus radiation . . . . .	3	1
Radiation only . . . . .	4	4

the 50 per cent or so of cures reported by him appeared to justify it. On the other hand, in the 30 cases reported by Watson and Gusberg, no such radical plan was followed, the procedures employed being often far more conservative than would be employed by most gynecologists, as can be seen from their Table III. And yet their results are much better than most authors have reported with the employment of vulvectomy and bilateral inguinal adenectomy, and not a great deal less favorable than those reported by Taussig with the more formidable Basset operation. This is rather confusing, and the only explanation that suggests itself is that their group of cases must have included a disproportionate number of less malignant types, such as the basal cell variety. However, the experience in our laboratory would indicate that the basal cell variety is relatively uncommon, and this appears to be that in other clinics. Whatever one's feelings may be about the advantages of the Basset type of operation, involving as it does, in one or two stages, extensive dissection of the intrapelvic lymphatic nodes, one must recognize that it is often contraindicated by the feeble and debilitated condition of these patients, most of them old women.—Ed.)

## SARCOMA OF THE VAGINA

W. K. DIEHL AND J. S. HAUGHT

Am. J. Obst. &amp; Gynec., 52: 302-310, 1946

Sarcoma of the vagina, like sarcoma in general, is a highly malignant tumor of mesoblastic origin. It is classified in 2 main types, childhood and adult. The botryoid is the more common childhood form, while the parietal is the more common adult variety. The botryoid variety (grossly appearing in grapelike clusters) in children is thought to develop from misplaced embryonal, mesodermic cells. A bloody vaginal discharge is usually the first symptom. As the condition progresses, the bladder frequently becomes involved, and death usually results from toxemia, uremia and exhaustion. In the adult, the typical vaginal sarcoma consists of bundles of spindle cells dispersed through a highly vascular stroma, with moderately numerous mitotic figures and hyperchromatic nuclei. The symptoms appear as a vaginal discharge, followed by ulceration, bleeding and infiltration of the vesicovaginal and rectovaginal septa. The disease terminates in a manner similar to that in children, although less rapidly.

Complete surgical excision is usually impossible and, while the tumor is radio-sensitive, recurrences rapidly develop. The prognosis is uniformly poor, and the diagnosis is questionable in any case which survives more than 2 years.

The authors present 2 case reports; the first represents a classical example of sarcoma botryoides in a 21 month old child. Death occurred within one year of the onset of the first symptom. The second is a case of adult vaginal sarcoma in a 40 year old Negress, treated by excision and radium application. Subsequent examinations show a gradual local regression of the growth. 6 figures.

(The rare sarcoma botryoides is a highly malignant and practically always fatal tumor. In most cases, as the authors state, teratomatous elements can be found, usually in the form of striped muscle tissue, often of embryonal type, so that it is not always easy to demonstrate microscopically. Cartilage may likewise be demonstrable in some cases. Vaginal bleeding in infants or young children should always be investigated. Sarcoma botryoides is always a possibility, though more frequently some other cause will be revealed, such as a foreign body in the vagina.—Ed.)

## THE UTERUS

### IMPORTANCE OF THE CONCEPTION OF METROSIS

AMERICO STABILE AND A. POU DE SANTIAGO

Arch. Urug. de Med., Cir. y Especial. (Uruguay) 28: 367-375, 1946

The use of the term "Metrosis" created by Conil-Mosinger (1935) is advocated by the authors to designate every correlative ovarian-endometrial pathological condition having no inflammatory basis nor neoplastic character.

Therefore, under the designation Metrosis the following conditions are included: 1) Metropathia hemorrhagica (glandular cystic ovarian metropathia of Pou Orfila); 2) Persistence of the corpus luteum (Halban's or Douay's disease); 3) Anovulatory bleeding; 4) Polyhormonal amenorrhea; 5) Moricard's metrosis of receptivity; 6) Atrophic type of metropathia hemorrhagica (Martinez Olascoaga).

All these conditions are caused by some sort of abnormality occurring in the ovarian-endometrium relationships, and they may or not be accompanied by metrorrhagias.

Many of them have been considered by different investigators just as simple clinical forms of the so-called metropathia hemorrhagica (Schroeder-Pankow), thus giving rise to great confusion in the literature as to the real meaning of the latter disease.

Therefore, in order to avoid such misconceptions, the term metropathia hemorrhagica (Pankow) should be applied only to the condition described by Schroeder, i.e., the one associated with glandular cystic hyperplasia of the endometrium and persistence of a mature follicle in the ovary, which, as a matter of fact, constitutes one of the main types of metrosis.

The so-called "metrosis of receptivity (Moricard)" refers to cases of amenorrhea with atrophic endometrium, despite the hormonal secretion being maintained at a normal level and, occasionally, even in excess (in the blood and urine). In such cases the endometrium does not seem to respond to the ovarian hormonal stimuli, which are within normal qualitative and quantitative limits.

(I have referred on a previous occasion to the penchant of our colleagues in South America for the use of proper names in the designation of diseases and operations, although we ourselves are not altogether free of this eponymic tendency. Where priority in the description of a new disease entity or a rare new operation is clear and unmistakable, it may be considered desirable, since it pays a well-deserved tribute to the memory of the discoverer. The names of such men as Addison, Graves, Froehlich, Wertheim, Gilliam and a host of others carry definite significance to clinicians in one field or another, since they at once convey to the mind the diseases or operations with which such men are intimately associated, just as pioneers like Hunter, Willard and Gasser have been similarly immortalized in the field of anatomy. But it does seem that our good friends to the south carry this practice too far and perhaps too indiscriminately. I wonder how many, if any, of us had heard of Douay's disease, or the metropathia of Pou Orfila, or Moricard's metrosis, all enumerated

by the authors of this paper. And yet they all refer to relatively common disorders encountered by all gynecologists, as you learn in the abstract of their paper. They evidently like the term "metrosis"—I wonder why they didn't call it the Conil-Mosinger disease—but it is such an all-inclusive one that it really does not seem to mean much.—Ed.)

## CONGENITAL GENITO-URINARY MALFORMATION AND ENDOMETRIOSIS

NORMANDO ARENAS AND OSCAR BLANCHARD

Boletín de la Sociedad de Obstetricia y Ginecología de Buenos Aires,  
25: 17-21, 1946

This is a case report. The patient, a single girl, 19 years old, came to the outpatient department complaining of a foul, abundant, yellow, thick vaginal discharge which began eight months prior to the consultation. Since she was 17 she had indulged in sexual intercourse.

Menstruation began at twelve, type 3-5/25-26, normal in every aspect. The patient looked emaciated and pale. Thorax, negative. Abdominal palpation entirely negative; both kidneys eluded palpation. The external genitalia were hypoplastic. The vagina was small, with diminished elasticity. All along the right side of the vagina there was a swelling that caused the right wall to bulge. The swelling was connected to a mass in the pelvis which seemed cystic and tender. The cervix, infantile, pointed toward the posterior fornix. The corpus uteri was small and anteflexed.

A puncture of the swelling was performed and yielded abundant pus, stained with blood. The possibility of a congenital genito-urinary abnormality was considered and studies were performed. Hysterosalpingography revealed a left uterus unicornis.

Cystoscopy revealed the absence of the right ureter and the presence of two ureteral meatuses on the left. Indigocarmine excretion was normal. Intravenous urography revealed two left kidneys fused in the vertical line, with independent pelves and ureters. Operation was decided upon. The abdomen was opened and a double uterus was exposed, with marked transverse development. Both uterine bodies were fused at the level of the isthmus. As the right uterus was connected with the blind right vagina, with pyocolpos, a right hysterectomy was performed. Later, through the vagina, the vaginal septum was extirpated. The patient had a stormy post-operative course and died eight days afterward, apparently from an acute embolism.

The anatomopathological study was performed by Prof. Rodolfo Sammartino. The sections of the cornu uterinus revealed a normal myometrium, while the endometrium was proliferative and showed signs of endometritis. The vaginal septum was composed of connective tissue and was lined on one side by normal vaginal epithelium and in the other by leucoplaquic epithelium (parakeratosis), subacute inflammation and glands partially mucinous.

*Note of the abstractor:* In no part of the article was endometriosis mentioned; the only explanation I can find for the title is that what the authors called endometriosis is the endometrium of the right cornus uterinus which was not in connection with the outside and that showed endometritis.

(The title of this paper seems inaccurate, because nothing in the case report suggests an endometriosis in the accepted usage of the term. The condition described obviously represents a congenital anomaly involving chiefly the right Müllerian canal. There was evidently a failure of fusion of the two Müllerian ducts in their upper portions, since the uterus was of the bicornate variety. In their vaginal portions the ducts also failed to fuse, while the right canal ended blindly because it failed to open into the urogenital sinus. This brought about a hematocolpos on the right, and as a result of secondary infection, the characteristically bloody content became converted into the blood-stained pus which was evacuated in the puncture described by the authors. Certainly there would seem to be no justification for applying to such a condition the designation of endometriosis.)

An interesting feature of the case was the renal fusion revealed by pyelography. The practical point to emphasize is that anomalies of the genital canal are often associated with anomalies of the urinary tract, especially congenital absence of the kidney or pelvic kidney. Pyelography should be a routine part of the examination of patients presenting genital canal anomalies.—Ed.)

## PRIMARY LIPOMA OF UTERUS

W. J. REICH AND M. J. NECHTOW

Am. J. Obst. & Gynec., 52: 157-159, 1946

The rarity of lipomas in the uterine wall may be ascribed to the lack of fatty cells in the muscle wall. A review of the literature for the past 25 years reveals only 4 cases of uterine lipoma; 2 were fibrolipomas and 2 were small lipomas. In the world literature from 1816 to 1921 only 26 lipomas were recorded. Although they are said to occur nearly always after the age of 60, the present case report deals with a patient of only 39 years.

The exact origin and pathogenesis of uterine lipomas is not certain. Various workers believe that they are a transformation of muscle fiber into fat, that they originate from embryonic cell rests, and that the fat cells around the uterine blood vessels may be the source. A. J. Peterson believes that microscopic sections may reveal other tissue mixed with the fat tissue.

The patient, a 39 year old Negress, whose case is presented in this paper, was admitted to the hospital with a history of a progressively enlarging abdominal tumor and menorrhagia. A large abdominal mass the size of an 8 months' pregnancy was noted. The mass also filled the entire pelvis and was firm and fixed. The preoperative diagnosis was uterine fibromyoma. At operation a large multinodular fibroid uterus was found. One of these nodes felt very soft on gross palpation. A supracervical hysterectomy and bilateral salpingo-oophorectomy were performed. The pathological report described multiple uterine fibromyo-

mas; one intramural encapsulated node appeared soft and yellow on cut section. Microscopically there were uniform areas of encapsulated fat and no mixture of muscle fibers. The diagnosis was lipoma of the uterus.

Clinically this tumor, by its softness, resembles a degenerated fibroid or a possible associated pregnancy. 2 figures.

(There appears to be little doubt that fatty degenerative changes may occur in rare cases of myomas, as well as sarcoma of the uterus, although the exact source of the fat, and the chemistry involved, are difficult to explain. One may even in rare cases see large areas of fat on naked eye examination, the true fatty nature of such tissue being confirmed by differential staining. In such cases one perhaps has to deal with mixed tumors, or lipomyomas, arising from "anlagen", so to speak, of two different tissue types.—Ed.)

### INFREQUENCY OF CARCINOMA OF THE UTERINE CERVIX AMONG JEWISH WOMEN

J. V. TREUSCH, A. B. HUNT AND A. A. ROUSUCK

Am. J. Obst. & Gynec., 52: 162, 1946

In a recent analysis of 568 consecutive cases of cervical carcinoma at the Mayo Clinic, it was found that in 566 instances the expressed religious preference of the patient was other than Jewish. In the remaining 2 cases it was impossible to classify the patient as Jewish or non-Jewish, but it did not appear that either was Jewish. The estimated Jewish registration by per cent of total at the Clinic is about 7 to 8 per cent. Therefore, one would have expected to find about 40 Jewish women in the present series. It is possible that one or more Jewish women of Christian religion was encountered unknowingly in this series, since it is estimated that about 4 per cent of the Jewish population are Christians. Nevertheless, this study brings forth the infrequency of carcinoma of the uterine cervix among Jewish women.

(The rarity of cervical carcinoma among Jewish women is generally recognized. There are many other instances of racial immunity or susceptibility to various diseases, such as the high incidence of uterine fibroids among Negroes, and of urinary calculi among the Chinese.—Ed.)

### AN UNUSUAL STRAIN OF NEISSERIA ISOLATED FROM THE CERVIX UTERI

MARION B. COLEMAN

J. Vener. Dis. Inform., 27: 159-160, 1946

Micrococci that had the properties of gonococci, including fermentation of glucose but not maltose, sucrose or lactose, were isolated from specimens of dis-

*Note of the abstractor:* In no part of the article was endometriosis mentioned; the only explanation I can find for the title is that what the authors called endometriosis is the endometrium of the right cornus uterinus which was not in connection with the outside and that showed endometritis.

(The title of this paper seems inaccurate, because nothing in the case report suggests an endometriosis in the accepted usage of the term. The condition described obviously represents a congenital anomaly involving chiefly the right Müllerian canal. There was evidently a failure of fusion of the two Müllerian ducts in their upper portions, since the uterus was of the bicornate variety. In their vaginal portions the ducts also failed to fuse, while the right canal ended blindly because it failed to open into the urogenital sinus. This brought about a hematocolpos on the right, and as a result of secondary infection, the characteristically bloody content became converted into the blood-stained pus which was evacuated in the puncture described by the authors. Certainly there would seem to be no justification for applying to such a condition the designation of endometriosis.

An interesting feature of the case was the renal fusion revealed by pyelography. The practical point to emphasize is that anomalies of the genital canal are often associated with anomalies of the urinary tract, especially congenital absence of the kidney or pelvic kidney. Pyelography should be a routine part of the examination of patients presenting genital canal anomalies.—Ed.)

## PRIMARY LIPOMA OF UTERUS

W. J. REICH AND M. J. NECHTOW

*Am. J. Obst. & Gynec.*, 52: 157-159, 1946

The rarity of lipomas in the uterine wall may be ascribed to the lack of fatty cells in the muscle wall. A review of the literature for the past 25 years reveals only 4 cases of uterine lipoma; 2 were fibrolipomas and 2 were small lipomas. In the world literature from 1816 to 1921 only 26 lipomas were recorded. Although they are said to occur nearly always after the age of 60, the present case report deals with a patient of only 39 years.

The exact origin and pathogenesis of uterine lipomas is not certain. Various workers believe that they are a transformation of muscle fiber into fat, that they originate from embryonic cell rests, and that the fat cells around the uterine blood vessels may be the source. A. J. Peterson believes that microscopic sections may reveal other tissue mixed with the fat tissue.

The patient, a 39 year old Negress, whose case is presented in this paper, was admitted to the hospital with a history of a progressively enlarging abdominal tumor and menorrhagia. A large abdominal mass the size of an 8 months' pregnancy was noted. The mass also filled the entire pelvis and was firm and fixed. The preoperative diagnosis was uterine fibromyoma. At operation a large multinodular fibroid uterus was found. One of these nodes felt very soft on gross palpation. A supracervical hysterectomy and bilateral salpingo-oophorectomy were performed. The pathological report described multiple uterine fibromyo-

## THE ADNEXA

### HUGE TUMORS OF THE OVARY

SYLLA O. MATTOS AND O. ALVES DE LIMA, JR.

Rev. de Obst. e Gin. de S. Paulo (Brazil), 7: 259-356, 1946

In this article the writers report 9 unusual cases of enormous ovarian growths, which they had the opportunity of studying in the last few years, stressing their rarity nowadays, and the difficulty in differential diagnosis with other intraperitoneal conditions, once the tumors fill the entire abdominal cavity. Despite the poor general condition of these patients resulting from the long existence of the tumor, in some as much as 10 and 30 years, the surgical results were excellent, all of the patients still being alive and in good condition.

With the great progress reached in gynecologic surgery and modern semiologic procedures, the occurrence of such enormous ovarian neoplasms has become exceedingly rare, since they are removed before they attain very great size.

In Kehrer's review of the literature from 1873 to 1928, 99 cases of huge ovarian tumors were reported. From 1928 up to 1944, the authors were able to collect 37 cases from the entire literature, although their size was not as large as those described in earlier days.

There are various opinions regarding when an ovarian tumor ought to be classified as huge, all of them based on the weight and size of the tumor. However, it seems more logical to consider a neoplasm as such whenever it fills the whole abdominal cavity, taking into consideration no limit of weight nor dimensions, since the same tumor may be huge for a small person and may be not so large for a big individual.

The authors discuss the clinical, pathological and therapeutic aspects of these tumors.

Usually they are cystadenomas, much more frequently of the pseudomucinous type, multilocular, and therefore, with a liquid mucoid content, which sometimes becomes dark and hemorrhagic with a gelatinous character. The typical high columnar epithelium is flattened due to the intracystic pressure. Much more seldom a serous cystadenoma, a dermoid cyst or an ovarian carcinoma becomes huge.

The cases collected from the literature occurred between the ages of 17 and 73, with an average of 42.3 years.

Physical and pelvic examinations yield no information whatsoever as to the origin of the tumor. A valuable aid for this particular purpose is given by the radiographic method of Mirizzi, with contrast of the gastro-intestinal canal. Hence, besides the dislocation noticed of the stomach, the small intestine (which sometimes encircles the tumor laterally and above) and the right colon, there occurs a flattening of the "S" sigmoid (Mirizzi's sign) which is important in deter-

charge from the cervix uteri of a 20 year old patient, collected on February 6, February 20, April 5, and August 2. Penicillin was administered on August 10 and 11. A culture taken on August 21 showed many convex, mucoid, transparent colonies with undulate margins typical of the gonococcus and reacting to the oxidase test. Subcultures produced no acid in ascitic fluid semisolid or in starch-gelatin agar containing glucose. No agglutination was obtained in antimeningococcus or antigonococcus serums that gave definite reactions with representative strains of the homologous *Neisseria*.

This micro-organism is considered to be an aberrant strain of either *Neisseria catarrhalis* or *N. gonorrhoeae*. If the latter, the fermentative properties may have been affected by penicillin. If it is a strain of *N. catarrhalis*, its colonial and cultural properties differ markedly from those considered characteristic for the species. This observation emphasizes the need for determining the fermentative properties of all species of *Neisseria* regardless of their source and other characters.

omy was performed and a huge ovarian cyst removed. The extraordinary growth attained by the tumor in 24 hours can be explained only on the basis of decompression following delivery, this allowing the neoplastic cells to secrete more, since no twisting of the pedicle had occurred.

In order to demonstrate the difficulty of establishing a correct diagnosis in such huge growths, the authors present 2 other cases. One of them had previously had a diagnosis of ovarian carcinoma, but on laparotomy the enormous growth was seen to originate from the omentum which, on pathological examination, proved to be a hemangiosarcoma. The genital organs showed no abnormality. Such tumors of the omentum are extremely rare, especially the huge ones.

The other case was thought to be a pregnancy associated with an ovarian cyst with twisted pedicle. However, later a diagnosis of hydramnios was made and an x-ray plate showed a twin pregnancy. As the symptoms became worse, the cervix was dilated, the amniotic sac emptied by puncture, followed by removal of 2 fetuses.

All cases of ovarian tumors were operated upon (puncture followed by removal of the tumor in 6 cases, simple salpingo-oophorectomy in 2 cases and bilateral salpingo-oophorectomy in one case) with success, and all of them are still living.

(As the authors state, the old-fashioned tumors were the biggest, and for the reasons mentioned by the authors in their interesting review of mammoth ovarian tumors, including their own group of nine cases. In the chapter on Mammoth Ovarian Tumors in the late Frank Lynch's monograph on Pelvic Neoplasms, the case of Spohn is spoken of as probably the largest on record, its weight being given as 328 pounds. As might be expected, it occurred in Texas, the big state of big things and big stories. However, this weight apparently included the weight of considerable fluid removed by tapping during the week preceding operation. In Lynch's collection of mammoth ovarian tumors were included no less than 10 over 200 pounds, though some of them are open to the same criticism as that of Spohn.

Every now and then at gynecological meetings, when someone reports an exceptionally large tumor, there follows a round of tumor stories not unlike fishing yarns, and perhaps no less mendacious. My own contribution at one of these orgies some years ago was to report a tumor of exceptionally fine quality, just imported from Germany, since I had removed a 55 pound pseudomucinous cystadenoma from a woman who had just come from Germany, bringing her tumor with her. I suppose I should have added that it was filled with Pilsener beer.

While serous cystadenomas may become very large, it is the pseudomucinous variety which, as the authors say, is most likely to attain mammoth proportions. The possibility of malignant change must always be borne in mind, and this cannot always be suspected from the external appearance of the cyst. For this reason, it is always wise to remove such growths without any spill of the contents, as is almost always possible. For that matter, even the cells of a histologically benign cystadenoma may plant themselves upon the peritoneum.

The authors have done a service in calling attention to the possible value in differential diagnosis of x-ray studies and hysterosalpingography. Incidentally, I wonder how many American gynecologists have ever heard previously of Mirizzi's sign?—Ed.)

mining whether the tumor arises from the pelvis, especially when it has a long pedicle and originates in the left adnexa. Therefore, following a barium enema, an x-ray picture is taken with the patient lying dorsally. When the pelvic tumor has a pedicle on the left side, the "S" segment of the sigmoid usually shows no contrast or just a very little thin fringe, due to compression of the neoplasm against its walls. A second plate is then taken with the patient standing up. The barium can then be seen filling the portion formerly empty, because the change of position brings about a decompression of the tumor.

Hysterosalpingography may also prove to be of help. The tube corresponding to the side of the neoplasm becomes much longer and is dislocated upward with the latter. The uterus, on the other hand, is dislocated downward and externally.

Great difficulty may be encountered in differential diagnosis, which ought to be made from: (1) other genital tumors (myomas, hydatid mole and pregnancy with hydramnios); (2) intra-abdominal tumors (ascites, mesenteric cysts, tumors of the omentum, spleen, liver, etc.); and (3) retroperitoneal tumors (kidney and adrenocortical tumors).

Treatment may consist of puncture followed by oöphorectomy, oöphorectomy not preceded by puncture, enucleation or marsupialization.

Puncture followed by removal of the tumor is a good procedure especially in the largest tumors, and whenever possible both should be done at one stage. If the case permits, puncture can be avoided and the tumor is removed through a long incision in order to dissect the multiple adhesions that usually exist. Enucleation can only very rarely be accomplished and marsupialization is resorted to only in extreme cases, such as those in which entire removal of the growth turns out to be impracticable. Preference should be given to local anesthesia, since most of these patients are in poor organic condition and have low resistance.

Finally, the authors report their 9 cases of huge ovarian tumors classified as pseudomucinous cystadenomas (7 cases), dermoid cyst (1 case) and solid anaplastic carcinoma (1 case). The age incidence varied from 12 to 79 years, the former constituting the youngest patient in the literature presenting a huge ovarian cystadenoma, and the latter the oldest one from 1928 to 1944, also with a cystadenoma. The heaviest tumor weighed 40 kg. (pseudomucinous cystadenoma) and contained around 25 liters of fluid. This case is interesting since the patient was a small woman weighing only 36 kg., i.e., the tumor weighed more than she did. The lightest tumor weighed 12 kg. and occurred in the small young girl.

One of the cases of pseudomucinous cystadenoma occurred in a woman having also a full-term pregnancy. Due to the enormous size of the abdomen, pelvic examination yielded no information, so that the possibility of acute hydromnios was borne in mind. Delivery occurred after the sac was perforated and very little liquid obtained. However, the abdomen still remained very large and the presence of a malignant growth with ascites was suspected. Within the next few days the abdomen became even larger and finally doubled in size in 24 hours. Therefore, a puncture was performed through the abdominal wall, yielding a gelatinous fluid. With a diagnosis of pseudomucinous cystadenoma, a laparot-

hand, pure forms of either granulosa or theca cells are rare. Both give rise to a hyperestrogenic syndrome, with often hyperplasia of the endometrium. Besides the transitional types, however, pure forms of granulosa and theca cell tumors can also be detected.

The coexistence of uterine cancer with metastases in one ovary and a simultaneous endocrine tumor occurring in the other ovary as is shown by this case, constitutes an exceptional event, perhaps even unique in the literature. The association of such conditions cannot be regarded as simple coincidence. As a matter of fact, there was in this case a localized area of hyperplasia of the endometrium just adjacent to the tumor, and it was probably caused by the hormonal activity of the thecoma cells. It is therefore logical to assume that, due to this persistent proliferation in a very sensitive area of mucosa, a cancer finally developed. This supposition is based upon the relation of hyperplasia of the endometrium to adenocarcinoma, as has been demonstrated by several investigators, particular stress being given to Novak's work, which points out this relationship in the postmenopausal group of cases. The writers do not mention at what age the menopause had occurred in their patient.

(The association of either granulosa cell carcinoma or thecoma with adenocarcinoma of the uterus is being reported with increasing frequency, and there can be no question that the relationship is a causal one. As a matter of fact, this occurrence offers additional testimony to the cancer-inciting possibilities of persistent estrogenic stimulation of the postmenopausal endometrium, which no longer undergoes cyclical change and which no longer is exposed to what may possibly be the protective influence of progesterone. While I have not studied the literature intensively, I believe that all or nearly all the reported cases have been in women beyond the menopausal age. In one or two cases in younger women the endometrial carcinoma appears questionable, the illustrations suggesting rather a benign though proliferative type of hyperplasia. Since our study on the relation between postmenopausal hyperplasia and adenocarcinoma (*Amer. J. Obst. & Gynec.*, 32: 674, 1936), I have seen a considerable number of instances of the coexistence of these lesions, and feel more and more that such postmenopausal estrogenic stimulation of the endometrium may at least predispose to the development of endometrial carcinoma.

We have encountered a number of instances of coexisting granulosa cell tumor and endometrial carcinoma in our own laboratory. The most recent American review of the subject, and it is a very good one, is that of Ingraham, Black and Rutledge (*Amer. J. Obst. & Gynec.*, 48: 760, 1944).—Ed.)

## DYSGERMINOMA OF THE OVARY

DANIEL A. ROJAS

Boletín de la Sociedad de Obstetricia y Ginecología de Buenos Aires,  
25: 33-54, 1946

The author presents four cases of dysgerminoma of the ovary. From the analysis of the cases published the author thinks that as yet no one can make

## THECA TUMOR OF ONE OVARY ASSOCIATED WITH A CARCINOMA OF THE UTERINE BODY SHOWING METASTASES IN THE OTHER OVARY

P. GUERIN, M. GUERIN AND A. TAILHEFER

Bulletin de l'Association Française pour l'Etude du Cancer, 33: 36-47, 1946

The authors report an interesting case of thecoma of the ovary coexisting with a carcinoma of the endometrium, which brings up the question of relationship between both tumors and the hypothesis of cancerization of the uterine mucosa under the influence of a hormonal substance secreted by the ovarian tumor.

*Case report:* 69-year-old woman, with 2 children, complained of metrorrhagia for 7 months. Pelvic examination revealed only a slightly enlarged uterus. A diagnostic curettage showed an adenocarcinoma of the endometrium. Pan-hysterectomy and bilateral salpingo-oöphorectomy were performed.

*Pathology:* Grossly, a tumor mass could be seen localized in the endometrium, toward the fundal portion. Left ovary showed a mass the size of a plum, and very soft. Right ovary was enlarged, the size of a walnut, firm in consistence, white-yellowish, and on cross section presented a fibromatous aspect with several yellow nodular structures.

Microscopically the uterine tumor was diagnosed as a papillary adenocarcinoma. It grew mainly toward the surface, and, therefore, there was only slight invasion of the myometrium. Adjacent to it, the endometrium presented an area of typical cystic glandular hyperplasia, whereas the remaining portions distant to the tumor showed no abnormality. In the left ovary there was metastasis of the uterine carcinoma, which destroyed the ovarian substance entirely. The right ovary showed confluent nodular areas of sarcoma-like cells, spindle-shaped or polyhedral in form, in connection with the ovarian stroma. Their cytoplasm was clear or slightly pinkish and contained lipid substances. The nuclei were round or oval, with few abnormalities, and mitoses were exceedingly rare.

Surrounding the tumor there was still some ovarian tissue and it was possible to trace the tumor cells directly from the stroma, which, due to their rich lipid content, resembled very much the theca cells. Silver impregnation revealed reticular fibers especially among the spindle cells, whereas they were rare in the areas of polyhedral cells. In the latter, on the other hand, the lipid content was shown to be much more marked. A diagnosis of theca-cell tumor of the ovary was made. Two years have elapsed since the operation was performed and the patient is still alive and in excellent condition.

The authors discuss the relationship between thecoma and granulosa cell tumors, asserting that lately there has been a tendency to include both tumors into a single group, in view of their embryologic, morphologic, histo-chemical and functional similitudes. In fact, as has been stated by Novak and others, granulosa and theca cell tumors have a common origin from the ovarian mesenchyma. Usually one sees tumors containing both types of cells and, on the other

## ANOTHER CASE OF ARRHENOBLASTOMA

A. H. CURTIS

Am. J. Obst. &amp; Gynec., 52: 128-132, 1946

The author describes the 3 arbitrarily distinguished types of arrhenoblastoma as follows: (1) the highly differentiated testicular adenoma of Pick; (2) the undifferentiated, chiefly sarcoma-like, functionally most active growth, diagnosed by rudimentary tubules and sex-like cords of cells; and (3) the intermediate group of large size and presenting great variation in structure, occupying a midposition as to function. The tumor in the present case belongs to the last-named group.

The patient, aged 52 years, had had amenorrhea for 6 months, with hoarseness of the voice and increasing distress and fullness of the abdomen. There was marked hirsutism, hypertrophy of the clitoris and abdominal enlargement suggesting arrhenoblastoma. Palpation revealed solid tumors, apparently of ovarian origin, extending to the level of the umbilicus, and an essentially normal uterus.

At operation both ovaries were found converted into solid tumors, each the size of a child's head. The uterus, tubes and ovaries were removed. The uterus contained 2 subserous myomas and the endometrium was more atrophic than normal in a patient only 6 months beyond her last menstrual period.

Grossly, the ovarian growths were markedly but smoothly nodular and red in color with some gray-white areas. Cut surface of one tumor showed irregular extensive areas of gelatinous softening; the other tumor was only slightly necrotic. Microscopically, the structure was a richly cellular alveolar configuration, this sarcoma-like tissue merging in places with irregular tubules and cords of epithelial cells, some with a distinct lumen and others in solid strands. A definite transition was noted from the richly cellular growth to spindle-shaped stroma cells, richly fibrotic tissue constituting a considerable portion of the tumor structure. The bilateral occurrence of this growth is unusual.

Since operation the patient's voice has modulated, hypertrichosis has largely disappeared and the clitoris has returned to normal size. 4 figures.

(See comment on following abstract.—Ed.)

## ARRHENOBLASTOMA OF THE OVARY; REPORT OF TWO CASES

M. T. GOLDSTONE

Am. J. Obst. &amp; Gynec., 52: 123-127, 1946

The subject of the first case presented in this paper was a 25 year old woman who had not menstruated for 2 years and who complained of dyspareunia (at-

definite statements about the characteristics or clinical evolution of these cases, and that their malignancy has been overestimated in some publications.

Three of the patients were less than 20 years old (15, 19, and 19) and one was 26 years old. The genitals were normal and so was menstruation in the four patients.

Three of the patients were virgins. One, a girl of 19, was married and had had two pregnancies. In all cases the tumor grew rapidly, the patients being aware of the rapidity of the growth. In three cases the tumor was larger than the head of a fetus and in one case larger than the head of an adult. In two of the cases there were adhesions to the intestines and pelvic walls.

In three of the cases a subtotal hysterectomy with bilateral adnexectomy was performed. In one, only the ovarian tumor was removed.

No x-ray radiation was given either before or after the surgical procedure.

The subsequent course of all 4 patients has been uneventful. Two of them were operated upon more than four years ago, one more than three years and one was operated upon last year.

The article includes the clinical histories of the four patients and the histopathological diagnosis is documented with microphotographs. In the discussion of this case Dr. Jorge Luis Ahumada said that from the revision of the world literature by him and Dr. Sardi in 1939, of the 159 cases collected only 16 (10%) were given as cured after five years. In one of his own cases recurrence occurred 10 years after the operation. He thinks also that in all cases of dysgerminoma intense deep x-ray therapy to the ganglions of the lumboaortic and pararenal chains must be instituted. The original tumor as well as the metastases are very sensitive to radiation and it is well known that it spreads generally through the lymphatic vessels.

(All these patients were young, and this is characteristic of dysgerminoma, which most often affects young girls in their teens or twenties, so that it has, at times, been spoken of as "carcinoma puellarum". There is an apparent difference of opinion as to the degree of malignancy of this tumor group between the author and the discussor, Dr. Ahumada, and a compromise viewpoint is probably more nearly correct. The former thinks that the malignancy of dysgerminoma has been exaggerated, while Ahumada finds that only 10 per cent of 159 reported cases were followed by a 5-year cure. I do not believe that this figure is accurate, and feel that some error has crept into Ahumada's statistics. No extensive follow-up studies of dysgerminoma are as yet available, but a recurrence rate of something like 25 to 30 per cent would seem to be more in line with reported experiences up to date.

On the other hand, I feel that the author takes these tumors too lightly. While even unilateral adnexal removal has cured a good many cases, especially those of small size still well-encapsulated, others have not been cured even by radical operation. These tumors tend sooner or later to break through their capsules and may infiltrate surrounding tissues extensively. The whole group, and this applies to other members of the dysontogenetic group (arrhenoblastoma and granulosa cell carcinoma) must be viewed as potentially if not actually malignant. In this relatively young group of patients, it is certainly justifiable to perform only unilateral adnexectomy if the tumor is small and well-encapsulated, and the conservative purpose of such a limited operation would be nullified by such postoperative deep x-ray therapy as Ahumada recommends. The importance of long-continued follow-up of all such cases is obvious.—Ed.)

The author believes that the high red blood counts in these 2 cases, which were not consistent with the low metabolic rates and large weight gains, constitute an important diagnostic feature of these growths. 2 figures.

(The 2 cases of arrhenoblastoma reported by Goldstine, and the one reported by Curtis, emphasize that these tumors are being diagnosed and reported with increasing frequency. While they must still be looked upon as rare, I would estimate that there must be close on to 125 instances in the literature, although I have not counted them recently. All 3 of the above cases appear pretty typical.

An interesting and not characteristic feature of one of Goldstine's cases was the marked increase of weight, which has also been noted in some of the adrenal tumors of the ovary, so that the syndrome has in some cases been described as resembling Cushing's disease. To my mind this suggests that the sex changes of arrhenoblastoma may really be explained by some interrelationship with the adrenal, though we know nothing as to its nature.

The original concept of Robert Meyer, explaining the biological effects of arrhenoblastoma simply on the basis of its histogenesis from certain originally male-directed cells in the region of the rete, has never seemed to me to be the whole story. Embryologically there is an intimate relation between the adrenal cortex and the ovarian medulla, this again suggesting an influence of the former in the abnormalities of sex differentiation seen with arrhenoblastoma. We shall have to learn a lot more about the mechanism of sex differentiation before we can expect to explain the significance of the sex changes seen with either ovarian or adrenal tumors.

Goldstine calls attention to the polycythemia seen in his two cases. This is certainly not a constant feature but it has been reported by others. Here again one is led to think of a cortico-gonadal relationship, as polycythemia is a frequent finding in Cushing's syndrome, which may be produced by adrenal cortical adenomas as well as by basophilic adenoma of the pituitary.—Ed.)

## THE ORIGIN OF ADRENAL-LIKE TUMOR OF THE OVARY (HYPER- NEPHROMA OF OVARY, ADRENAL TUMOR OF OVARY, MASCULINOVOBLASTOMA, LUTEOMA, LUTEINOMA)

A. H. CURTIS

Am. J. Obst. & Gynec., 52: 115-122, 1946

Only 15 well-authenticated cases of adrenal-like tumor of the ovary, besides the one presented herein, have been reported in the literature. All but one of these tumors have been unilateral, and nearly all have been small nodules not larger than a walnut. The growth is usually buried in the ovary, its protruding surface covered by a thin layer of ovarian tissue. Grossly, the tumor is solid, rubbery and ovoid; the predominant color is orange-yellow. Microscopically, the tumor consists of large, polyhedral eosinophilic cells disposed in cords, nests and anastomosing strands. They occupy the spaces of a network formed by capillaries. Stroma is usually scanty. The cells have distinct outlines, granular protoplasm, chromatic rather than vesicular nuclei and, invariably, nucleoli are present. There is usually considerable lipid material. All of these tumors present masculinization symptoms of amenorrhea, hirsutism and hypertrophy

tributed to a growth between the labia) and a pronouncedly masculine change of voice. She had gained between 40 and 50 pounds in 4 years and there had been a growth of hair on the face, arms and legs.

General physical examination was negative. Pelvic examination revealed that the clitoris was enlarged to 7 cm. in length and 3.5 to 2 cm. in width. The other pelvic organs were normal except that a tumor, the size of a tennis ball, occupied the site of the right ovary. The red blood count was 5,430,000 and the basal metabolic rate was minus 20. A diagnosis of masculinizing tumor of the right ovary was made.

At operation both tubes, the left ovary and the uterus were found normal. The right ovarian tumor was removed. Grossly, this tumor was smooth, regular, yellowish gray and quite firm, except for a cystic portion which occupied about  $\frac{2}{3}$  of the mass. This cystic portion contained straw-colored fluid. The cut surface of the tumor was homogenous in appearance and of light yellowish tan color. Microscopically the only definite arrangement was in the form of zigzag cords of elongated cells which tended to extend at right angles to the direction of the cords. Narrow spaces appeared about these unit structures which formed a network about areas of less deeply staining stroma where interstitial cells appeared. The stroma was quite vascular. Definite alveolar or tubular arrangement was absent. The diagnosis was undifferentiated arrhenoblastoma of the ovary.

The patient resumed normal menstruation postoperatively, lost weight, and the excessive growth of hair fell from her face, arms and legs. Her voice improved and the clitoris decreased in size so that there was no dyspareunia. The red blood count was 4,120,000 and the basal metabolic rate plus 2. Subsequently she had a normal pregnancy and parturition.

The second patient, a 20 year old woman, complained of amenorrhea for nearly one year, rapid weight gain and excessive hair growth on face and body. The clitoris was enlarged to 3 or 4 times its normal size, and the right ovary was palpable and enlarged. The red blood count was 5,510,000 and the basal metabolic rate was minus 18.

At operation the uterus, tubes and left ovary were found to be normal. The right ovary was the size of a golf ball, prolapsed and firmer than normal. The ovary was removed. Grossly, its surface was regular, except for small bulging cysts. A cut through the center showed a sharply demarcated tumor mass, homogenous and of light yellowish tan color. It was not encapsulated from the ovarian substance. Microscopic examination showed cordlike masses of deeply stained tumor cells composed of both acinar and tubular structures. The nuclei of these cells were mostly central and had a pyknotic appearance. In places the epithelial positions of the tumor narrowed to cords which took a zigzag course through zones of fairly dense fibrous stroma. The cells of these cords were at right angles to the direction of the cords. The nuclei of the stroma cells maintained the oval shape typical of newly formed fibrous tissue. Interstitial cells could not be recognized. The diagnosis was highly differentiated arrhenoblastoma of the ovary with testicular adenoma of Pick.

Postoperatively the patient resumed normal menstruation and lost weight and face and body hair. She subsequently became pregnant.

adrenal-like tumor of the ovary is an epithelial growth originating from dormant cells and that it cannot arise from stromal tissue is contrary to evidence produced by various workers. It is inferred that interstitial cells may really be identical with ordinary ovarian stroma cells.

It would appear that adrenal-like tumors of the ovary arise by metaplasia of stroma cells or other indifferent cells rather than from embryologically misplaced tissue in the ovary. The growth is comprised of luteinized epithelioid and spindle-shaped cells; whether the cells are to be called epithelial is arbitrary. It seems that no distinction should be made between adrenal-like tumor and luteoma or luteinoma of the ovary. 6 figures.

(The case reported is fairly typical of this rare variety of ovarian tumor. The clinical syndrome is much like that produced by arrhenoblastoma, although there have been some differences in a few reported cases in which the clinical picture was somewhat like that of Cushing's disease.

The hypothesis suggested by the author for the histogenesis of these tumors is of interest, although to me at least it lacks the ring of plausibility. With such tumors as granulosa cell carcinoma and arrhenoblastoma there is increasing reason to believe that they arise in the ovarian mesenchyme, and this seems logical since they represent neoplastic efforts at reproducing the structure of the gonad. But the adrenal tissue of which some ovarian tumors are composed is an alien one to the ovary. Rather than explaining its origin from normal ovarian constituents, it would seem more logical to theorize that since the ovarian and adrenal "anlagen" are almost continuous in the young embryo, cells of adrenal type may, so to speak, be trapped in the ovarian area, and later give rise to adrenal ovarian tumors. It is hardly worthwhile to belabor any of these hypotheses in the present state of our knowledge, or to enter into a discussion of the tumors designated as luteomata, or of whether or not a true luteoma can bring about masculinizing effects. Aside from our ignorance of the forces concerned in sex differentiation, the great difficulty lies in our inability to determine the exact type or source of the constituent tumor cells by histological methods, so that our conclusions are based largely on morphological evidence.—Ed.)

## BILATERAL CONCOMITANT FIBROMA AND SEROUS CYSTADENOMA OF THE OVARY

S. M. COPLAND AND F. C. COLEMAN

*Am. J. Obst. & Gynec.*, 52: 141-146, 1946

The case is presented of a 70 year old married woman whose complaint was swelling of the abdomen which, on admission, was the size of a full-term pregnancy. At operation the only structure visible was an enormous cyst, estimated to weigh about 20 pounds. About 3 quarts of clear, slightly straw-colored fluid was aspirated from the cyst and, as the cyst had developed from the left ovary, the left ovary and tube were resected. This specimen consisted of the collapsed cyst wall plus a hard firm piece of tissue. There was then noticed a cyst, about the size of a large indoor ball, in the right ovary; at the base of this cyst was a hard concrete-like mass. The cyst was deflated by aspiration and the right tube and ovary were resected.

of the clitoris. Some cases have also had glycosuria, polycythemia and hypertension.

The case reported by the author concerns a 23 year old patient with complaints of infertility, amenorrhea for 6 years, acne, hirsutism and lowered voice pitch. Examination revealed marked universal hirsutism of body surfaces and a greatly enlarged clitoris. The blood pressure was 125/80; there was no glycosuria. There was a polycythemia of 5,480,000. At operation a small, rather firm orange-yellow tumor was found in the right ovary, which was removed. The rest of the pelvis appeared normal, except for a notably small left ovary. Menstruation was resumed following operation, and the patient became pregnant. When she was last seen, prior to labor, there had been no significant change in hypertrichosis and the voice was somewhat husky. The acne had improved and the clitoris returned to normal size.

The tumor comprised about  $\frac{2}{3}$  of the ovary and was surrounded by a crescent of ovarian tissue. It was buried in the ovarian tissue, protruding disc-like from it. The tumor surface was granularly smooth, grossly resembling adrenal tissue or tumor of the corpus luteum. The growth was lobulated by fibrous septa radiating from the capsule. Microscopic examination revealed massive strands, wedge-shaped areas and isolated clusters of cells arranged in acini, also cord-like patterns and anastomosing networks. All of these were polygonal cells with a rich sinusoidal blood supply. The individual cells were clearly demarcated, had sharply outlined chromatic nuclei and small, deeply staining nucleoli. The stroma-like, greater bulk of the tumor consisted of lightly staining spindle-shaped cells and had a scant blood supply. Here the cell boundaries were less clearly defined, with a fine collagenous network of intracellular fibrils. The nuclei manifested a tendency to deviate, with the stroma, into a stromatogenous pattern. In many areas of the tumor there was a clearly defined transition from the adrenal-like polygonal epithelioid type of cells to the spindle-shaped type of cells. Fat, chiefly intracellular, was present in considerable amount; most of it was found in necrotic areas (which are a feature of this tumor).

The tumor capsule merged in many places with the ovarian stroma. In the ovary, some ova were seen as well as some larger follicles with marked luteinization of both granulosa and theca. The stroma was richly cellular, consisting of actively proliferating spindle cells. Whatever stimulated the tumor growth evidently had a similar effect on the ovarian stroma.

The author summarizes the available evidence concerning the nature of adrenal-like tumors. The rarity of adrenal rests in the ovary makes questionable such origin of adrenal-like tumors; also, only malignant tumors of the adrenal produce virilism, whereas adrenal-like tumors of the ovary are essentially benign. The theoretical possibility of luteinization in a pre-existent granulosa or theca-cell tumor in explanation of this masculinizing growth has brought forth much speculation.

Authentic adrenal-like tumors of the ovary all seemingly develop within the substance of the ovary, as though produced by a perverted physiologic process, rather than originating as an independent growth. The assumption that

late rapidly in large amounts, requiring more frequent aspirations than effusions of other etiology. The condition is most common between the ages of 40 and 60, the majority occurring after the menopause. The pathology of the ovarian tumor, with the exception of 2 cases, has been reported as benign fibroma. In the 2 exceptions, the syndrome occurred in a case of thecoma of the ovary, and in a case of multilocular papillary cystadenocarcinoma.

The authors present the case of a 61 year old woman who presented herself with the complaints of cough, shortness of breath and weakness. There was evidence of massive pleural effusion on the right with marked shift of the heart and mediastinum to the left. Because of the patient's extreme obesity and very large pendulous abdomen, it was not until 100 days after her admission that the ovarian tumor was discovered. During the weeks preceding operation it was necessary to aspirate the chest fluid daily; the average daily amount aspirated was 1500 cc. Also during her preoperative course in the hospital, ascites and edema of the legs developed.

Following removal of the tumor (a typical hard fibroma with a central area of hemorrhage and a little necrosis), epigastric distress and edema of the legs disappeared. She required no further chest aspirations; the chest fluid rapidly disappeared and the lung re-expanded.

(This interesting syndrome, originally thought to be characteristic of fibroma, has been found also in association with other solid ovarian tumors. Cases have been described in association with carcinoma (with no pleural metastasis), granulosa cell tumor, thecoma and Brenner tumor. There is still no clear-cut knowledge of the mechanism involved, though there has been much conjecture and some experimental work on the problem. Probably the best discussion of the subject, although it reaches no definite conclusions, is that of Rubin, J. Novak and Squire, published in the *Am. J. Obst. & Gynec.*, 48: 601, 1944.—Ed.)

## LARGE OVARIAN CYST; REPORT OF A CASE

F. J. HOFMEISTER

*Am. J. Obst. & Gynec.*, 52: 133-134, 1946

This report is not presented primarily because of the size of the ovarian cyst, but in view of the interesting problem created by the length of time this patient's condition was undiagnosed.

A 58 year old woman, weighing 264½ pounds and with an abdominal circumference of 62 inches, complained of this tremendously distended abdomen for 34 years. During this period of time she had been seen by various reputable physicians for conditions varying from pulmonary tuberculosis with peritoneal tuberculosis, to decompensated heart disease.

On her present admission, a diagnosis of probable ovarian cyst was made. Slow decompression was made over a period of 56 days prior to laparotomy. The collapsed cyst which was removed at operation was diagnosed as a benign unilocular, serous cystadenoma.

Sediment from the centrifuged specimen of fluid was grayish-white and disclosed foam cells, polymorphonuclear leucocytes and cholesterol clefts.

The cyst from the left ovary was lined by a ciliated low columnar epithelium with small papillary projections into the lumen of the cyst. The right ovarian cyst was lined by ciliated columnar epithelium; no papillations were present.

The solid tumors consisted of spindle-shaped cells with single nuclei. These cells were closely packed with an occasional area where a large amount of intracellular substance was present. In some areas the cells were arranged in parallel rows; in others a mosaic pattern existed. Mitotic figures were very rare, and blood vessels were not numerous. No fat was apparent.

This case presents a combination of the most common benign solid ovarian tumor (fibroma) and the most common benign cystic ovarian tumor (cystadenoma), yet the combination is most unusual.

The origin and histogenesis of these tumors is discussed. A cystadenoma, as well as a fibroma, may originate in a Brenner tumor. In the present case there appears to be no resemblance to a Brenner tumor. 4 figures.

(From the authors' description one would get the impression that the two tumor types are merely coexistent but probably not histogenetically related. Since pseudo-mucinous transformation of the epithelium of Brenner tumors occurs in a comparatively small proportion of cases, even large pseudomucinous cysts may thus arise, though this is certainly not a common explanation of the histogenesis of such cysts. While serous cystadenoma has been said by some to have a similar origin in rare cases, I have not seen such an instance, nor does this explanation seem rational, from what is known as to the common origin of serous cystadenoma from the surface epithelium of the ovary. Finally, it should be emphasized that Brenner tumors grossly resemble fibromas, and that the fibromatous overgrowth may at times almost blot out the original epithelial rests characterizing Brenner tumors, so that often many blocks of an apparent fibroma must be made before one can exclude an origin from Brenner tumor.—Ed.)

## PLEURAL EFFUSION ASSOCIATED WITH OVARIAN TUMOURS (MEIGS' SYNDROME)

V. D. SCHAFFNER AND T. A. KIRKPATRICK

Canad. M. A. J., 55: 55-57, 1946

A review of the literature reveals only 31 cases of the syndrome of pleural effusion, ascites and ovarian tumor up to September, 1945. The pathogenesis, and actual causative factor or factors, are not understood. The symptoms are shortness of breath, feeling of tightness in the chest, occasional chest pain, occasional cough, vague gastro-intestinal symptoms and swelling of the legs. Physical examination reveals pleural effusion (usually massive and generally in the right chest), evidence of ascites, and a freely movable, pelvic or abdominal tumor. The fluid is a sterile transudate with a specific gravity ranging from 1.012 to 1.018, usually of clear amber color. The pleural fluid tends to accumu-

is a characteristic accompaniment of endometriosis, though it may be found in some cases. On the other hand, there is no doubt that an established endometriosis is influenced by the ovarian hormones much like the normal uterine mucosa. Even this is subject to some qualification, as the ectopic endometrium is not infrequently of immature type, and thus sensitive only to estrogen, but not to progesterone.

It is not always necessary to identify both glands and stroma in order to make the diagnosis of endometriosis. Either one of them, if typical, will warrant such a diagnosis. It would only add confusion to add such distinguishing terms as adenosis, stromatosis, or histiocytosis. It seems hardly necessary to comment upon the author's recommendation of the last named term, since it will quite certainly not be adopted.—Ed.)

## GENERAL HISTOPATHOLOGY OF ENDOMETRIOSIS

TOMAS PERRIN

Ginec. y Obst. de Mexico 1: 53-65, 1946

Before describing the pathological picture of endometriosis, the author reviews the well-known cyclical changes that occur in the endometrium. He thinks it wrong to divide structurally the endometrium into a parenchymatous or glandular portion and a stromal or interglandular portion, since both represent functional tissues and, therefore, both are parenchymas. The designation stroma should be reserved for the reticular and collagenous portions supporting the cells, vessels and glands. Nor is it correct to refer to the endometrial stroma as cytogenous tissue, since the latter indicates lymphoid tissue, which, on the other hand, only very slightly resembles the former morphologically.

The different histopathologic aspects of endometriosis in its various intra- and extra-peritoneal forms are described, from the small, superficial lesions to the well developed chocolate cysts. The simple finding of pigment-containing phagocytes in the borders of a tarry cyst does not warrant the diagnosis of endometriosis, as any other kind of extravasation of blood may lead to the same picture. On the other hand, when the typical structures are lacking, the presence of decidual-like or real decidual cells do seem to be of great diagnostic value.

A brief discussion of stromatous endometriosis follows.

(A satisfactory review of the subject. As the author states, pigment-containing cells may be found in other hemorrhagic lesions than endometrial cysts. However, when a cyst is surrounded by a layer of the typical large, polyhedral pigment-bearing pseudo-xanthoma cells, there will be little doubt of its endometrial origin. Moreover, by making additional sections, one will practically always find at least vestiges of the original endometrial lining. On the other hand, the presence of even real decidual cells, frequently seen in the ovaries of pregnant women, does not justify the diagnosis of endometriosis. Such ectopic decidua does not necessarily mean a pre-existing endometriosis. It is ordinarily a purely stromal response to the pregnancy hormones, similar to that seen at times on the posterior surface of the uterus, the uterine ligaments, the appendix, or omentum.—Ed.)

The total fluid removed during the 56 days and at the time of operation was 80,840 cc. and weighed 223 pounds. There was reaccumulation of fluid during this 56-day period. The cyst wall was not weighed, but it is safe to regard the combined weight of the cyst wall and fluid as in excess of 164 pounds.

(As the author states, it is remarkable how even very intelligent women may fail to notice abdominal or pelvic tumors of great size. Large ovarian cysts are apt to produce a fairly symmetrical enlargement which the patient is likely to interpret as abdominal adiposity, especially as there is usually no associated pain. But even the hard nodular myomas of large size not infrequently fail to attract the patient's attention. Not so very long ago I removed an ovarian cystadenoma of 25 pounds from a woman physician who was something of a gynecologist herself.

Whenever feasible, and it almost always is, even the large cysts should be removed intact, without previous tapping or aspiration. Even the cells of some histologically benign cysts have the capacity of implanting themselves on the peritoneum. On the other hand, one can never be sure from the external appearance of a cyst that it has not undergone malignant degeneration, and the hazard of peritoneal implantation is naturally much greater under such circumstances. The subject of giant or mammoth ovarian tumors was discussed in another paper by Mattos and de Lima, abstracted in this issue of the Survey (p. 897), with editorial comment.—Ed.)

## CLINIC OF ENDOMETRIOSIS

ROSENDO AMOR

Ginec. y Obst. de Mexico 1: 67-76, 1946

In this article, a clinical study concerning the symptomatology and diagnosis of endometriosis in all its different localizations is made.

Endometriosis seems to have a definite endocrine basis, with a certain degree of hyperestrogenism, which can be revealed by the blood tests and suspected by dysmenorrhea and other symptoms occurring cyclically before, during and after menstruation, menstrual disorders, etc., all of which regress with the set-up of menopause.

Differential diagnosis ought to be made from corporeal and cervical perimetritis of septic nature, hypertrophy of uterine body, sclerosis, fibroids, polyps, chronic pelvic inflammatory disease, etc. The past history may be of some help, as it can exclude a previous inflammatory disease.

Pathological diagnosis of true endometriosis is made by identifying both elements of the endometrium: glands and stroma. If either one of these is lacking, a diagnosis of adenomatosis or stromatosis is made. Better than the designation stromatosis should be the term histiocytosis, since it is made up exclusively by histiocytes.

A description of the well-known clinical picture of adenomyosis and endometriosis follows, nothing new being added.

(That the etiology of endometriosis is of endocrine nature has been thought by many, but proved by no one. Nor do I know of any evidence to indicate that hyperestrogenism

The remaining 20 patients were gonococcus positive preoperatively (by urethral and/or cervical cultures.). Twelve of these were treated successfully prior to operation, 10 with sulfonamide therapy and 2 with penicillin, and showed gonococcus negative bacteriological findings in their operative material. Two other patients were sulfonamide resistant. The remaining 6 gonococcus positive cases received no treatment at all; nevertheless, 2 patients became spontaneously negative bacteriologically preoperatively and yielded negative findings on their operative material. Thus, there were only 4 untreated and 2 sulfonamide resistant patients who had gonococcus positive bacteriologic findings of the urethra or cervix prior to operation. Gonococci were found in the operative material of 4 patients; 3 of these had not received any treatment, and one was resistant to sulfonamide therapy.

These findings indicate that gonococci persisted in the female adnexa in only 4 out of 8 untreated or treatment resistant cases and, in addition, negative findings in the operative material were obtained from 12 originally infected patients who were treated adequately preoperatively. Such findings suggest the value of administration of penicillin in adequate amounts to patients with pelvic inflammatory disease prior to operation, particularly in the presence of an antecedent history of gonococcal infection. Illustrative case reports are presented.

(The studies of Curtis (Surg., Gyn. & Obst., 33: 621, 1921) as far back as 1921, appeared to indicate a rapid disappearance of gonococci from the tubal tissues after subsidence of the acute symptoms, although the later work of Studdiford, Casper and Scadron (Surg., Gyn. & Obst., 67: 167, 1938) pointed to a much longer persistence of the infection. Both these studies were made before sulfa and penicillin therapy were available, and hence the paper abstracted above is all the more interesting, indicating as it does the great value of adequate penicillin therapy. There is still the problem of the sulfonamide and penicillin resistant group of cases, and our knowledge of this angle of the subject is still incomplete. Ed.)

## INTERPRETATION OF THE PATHOGENESIS OF PELVIC INFECTION AS DETERMINED BY CORNUAL RESECTION

H. C. FALK

Am. J. Obst. & Gynec., 52: 66-73, 1946

It is generally accepted that the gonococcus is the infecting organism in most cases of primary salpingitis. However, at operation, cultures of the tubes are either sterile or reveal other organisms. This raises the question as to whether the gonococcus prepares the tube for subsequent infection by other organisms, and as to how these secondary invaders reach the tube.

For the past 8 years it has been the practice at Harlem Hospital not to remove the tubes except when the ovary was involved. Instead, continuity of the tube, uterus and cervix was broken by resecting the cornual end of the tube and leaving

## TREATMENT OF ENDOMETRIOSIS

ARTURO DE LOS RIOS

Ginec. y Obst. de Mexico 1: 78-88, 1946

Since development of endometriosis is caused by estrogen, its therapy should consist in diminishing or abolishing the production of the latter.

In order to accomplish this purpose, three methods can be used:

1) The organotherapeutic procedure, which inhibits the secretion of estrogen while it is being applied, constitutes just a temporary form of treatment in young patients. Progesterone or testosterone can be used, especially the latter.

2) X-ray and radium constitute a blind procedure with very limited indications, and, moreover, it is radical.

3) Preference should be given to the surgical treatment, since its performance can be controlled by a correct diagnosis and, furthermore, the extension and localization of the lesions can enable the surgeon to choose a conservative or radical procedure.

Since endometriosis is a disease that occurs during the sexual life of a woman, the conservative procedures should be given preference as far as the ovarian function is concerned, taking into consideration the age of the patient, localization, extension and clinical picture of the condition.

(The author's conclusion that when treatment of endometriosis is necessary, which is not invariably the case, the surgical plan is the best, will be endorsed by all gynecologists. There are of course some exceptions, as for example, in cases of residual endometriosis knowingly left behind after properly conservative operations in comparatively young patients in whom future reproductiveness is an important consideration. If severe dysmenorrhea continues, which is not always the case, one can employ testosterone for its undoubtedly inhibitive effect upon the aberrant endometrium. But such treatment is very transient in its effect, and of course never curative. Moreover, most such patients can be made reasonably comfortable with such simple analgesics as codein and aspirin, which is cheaper and more convenient, without the well known disadvantages of long-continued testosterone therapy. I see no advantage in the latter, although it has been recommended by a number of authors.—Ed.)

## THE PERSISTENCE OF THE GONOCOCCUS IN THE FEMALE ADNEXA

A. COHN, I. GRUNSTEIN AND C. E. HEATON

Am. J. Obst. &amp; Gynec., 52: 83-88, 1946

The operative material of 65 hospitalized female patients suffering from acute or chronic adnexal disease was examined bacteriologically for the presence of the gonococcus. Forty-five of these women had persistent gonococcus negative bacteriological findings, both pre- and postoperatively, and also in their operative material.

The remaining 20 patients were gonococcus positive preoperatively (by urethral and/or cervical cultures.). Twelve of these were treated successfully prior to operation, 10 with sulfonamide therapy and 2 with penicillin, and showed gonococcus negative bacteriological findings in their operative material. Two other patients were sulfonamide resistant. The remaining 6 gonococcus positive cases received no treatment at all; nevertheless, 2 patients became spontaneously negative bacteriologically preoperatively and yielded negative findings on their operative material. Thus, there were only 4 untreated and 2 sulfonamide resistant patients who had gonococcus positive bacteriologic findings of the urethra or cervix prior to operation. Gonococci were found in the operative material of 4 patients; 3 of these had not received any treatment, and one was resistant to sulfonamide therapy.

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For the past 8 years it has been the practice at Harlem Hospital not to remove the tubes except when the ovary was involved. Instead, continuity of the tube, uterus and cervix was broken by resecting the cornual end of the tube and leaving

the rest of the tube in situ. As demonstrable organisms had disappeared from the tube after the temperature had been normal for 2 weeks, it was thought that the tube could not reinfect itself, but was infected through the cervix and uterus. If this concept were true, then cornual resection should prevent reinfection of tube. If, on the other hand, this concept were false and reinfection of the tube occurred from a latent or dormant infection of the tube wall, then cornual resection should not prevent attacks of recurrent salpingitis. Cornual resection has been performed in over 1000 cases with a follow-up of over 8 years, and in no instance is reinfection known to have occurred in any of these tubes. In 6 patients who were operated upon subsequently for fibroids or ovarian cysts, the tubes were removed for study. In no instance was it possible to demonstrate in these tubes, removed at least 9 months after cornual resection, any histologic evidence of acute or chronic inflammatory disease.

From this study and those of most other observers, it is evident that in patients who have had frequent attacks of salpingitis, the gonococcus had disappeared from the tube and other organisms replaced it. Since primary streptococcus and staphylococcus infection of the tube is infrequent, and since these organisms are prominent in pelvic inflammatory disease, it would seem that the tube infected by the gonococcus is more susceptible to these secondary invaders.

It is the author's belief that infection, whether gonorrheal, streptococcal or staphylococcal, ascends from the cervix through the uterus and outward into the lumen of the tubes. Otherwise, it is difficult to explain the absolute disappearance of tubal infection on performing cornual resection.

(In spite of the good results reported by the author, the method of cornual resection which he recommends does not seem to have achieved any great degree of acceptance. Most gynecologists will probably still prefer removal of the diseased tube to simple cornual resection, which is certainly no more conservative as regards the possibility of later pregnancy, and is not much simpler in most cases. Operations for tubal infection are far less common than formerly, and when done it is not because of existing infection but for the wreckage resulting from an infection long since past.—Ed.)

## FEMALE UROLOGY

### THE MUSCLE OF MICTURITION; ITS ROLE IN THE SPHINCTER MECHANISM WITH REFERENCE TO INCONTINENCE IN THE FEMALE

WILLIAM T. KENNEDY

Am. J. Obst. & Gynec., 52: 206-217, 1946

The author has concluded that further study of the anatomy and physiology of the urethra is necessary in order that the gynecologist may render adequate treatment in cases of female incontinence. In the present paper he presents certain information obtained from recent study of this organ.

A study of the urethra with serial sections, concentrating specifically on the intrinsic voluntary muscle fibers, revealed that they compose a single muscle, having an unusual function and shape. It has been temporarily named the *muscle of micturition*. It was found that the muscle of micturition has 2 origins, that it passes completely and obliquely as a purse string in the muscle wall around the middle and inner thirds of the urethra, and has 2 insertions into and among the smooth longitudinal muscles of the trigone. When relaxed, this muscle is shaped like an oblique cross section of a cylinder, but when contracted it assumes the shape of a normal straight cross section of a cylinder. A nerve from each pudendal trunk appears to pass to the muscle of that side near its origin.

When the muscle of micturition relaxes, the levator ani muscle contracts to lift the lateral wall of the urethra near the junction of the middle and inner thirds of the urethra, or the lateral wall of the cylindrical or true sphincter. The bulbocavernosus muscle contracts to pull down and compress the glandular portion. The transverse perinei contracts to give firm support to the urethra at the junction of the outer and middle thirds of the urethra. In this "relaxing state", the cylindrical or true sphincter is circular and possesses its greatest control. No urine runs out of the bladder. The muscle of micturition (the oblique voluntary purse-string muscle) exerts no distorting influence on the smooth muscle of the cylindrical sphincter.

When the muscle of micturition contracts, the levator ani muscle relaxes and allows the muscle of micturition to pull the lower wall of the inner third of the urethra down and out. The transverse perinei muscle is pushed outward, releasing any sphincter control. The bulbocavernosus muscle is pushed outward and up, and releases any sphincter control it may have had. The contracted muscle of micturition becomes circular to the urethra instead of oblique, and makes a new arrangement of the urethral wall. The inferior walls of the inner third of the urethra slide forward almost directly under the superior wall of the middle third of the urethra. None of the circular muscles which, in relaxation,

was directly across the axis from its mate is any longer so, but is now diagonally across, the result being a distorted cylindrical sphincter. The cylindrical or true sphincter is now open and permits escape of urine from the bladder. Any permanent degree of distortion means a similar degree of incontinence. At the same time the trigone is drawn toward the transversus inferior muscle of the muscle of micturition, and adhesions may permanently cause some degree of this elliptical formation and, therefore, some degree of incontinence.

Should the muscle of micturition become devoid of innervation, the cylindrical sphincter would remain closed, and only peristalsis or bladder pressure would carry urine out of the bladder.

It is concluded that, in order to obtain maximum restoration of continence, the operator should restore completely the relaxation of the muscle of micturition by putting the internal urethral meatus as far back in the pelvis as possible. He should restore as completely as possible the contracting power—at rest—of the levator ani, the transverse perinei and the bulbocavernosus muscles. He should restore as much as possible all damage inflicted upon the trigone, the adjacent bladder wall and the associated anterior vaginal wall, a procedure which is necessary for maximum efficiency of the cylindrical sphincter. To achieve continence of urine it is necessary to maintain this restoration. 12 figures.

(It is probable that a considerable proportion of even very able gynecologists and urologists have had very imperfect concepts of the physiology of micturition. For that matter, there has been no little confusion of thought on this subject among anatomists and physiologists themselves. The author has long been a worker in this field, and his past contributions, especially as they bear on the subject of stress incontinence, are well-known. The Kennedy operation for the correction of this condition has been widely adopted, and its usual effectiveness recognized.

The anatomical studies described in the present paper cannot be intelligently evaluated by the average clinician, and it will be interesting to see how they are received by the anatomists, since the author has introduced certain new concepts, especially as to the "muscle of micturition". It is refreshing, however, to note that the desiderata of operations for incontinence, as emphasized by him, do not clash with the principles employed by most gynecologists, especially as to the importance of "putting the internal urethral meatus as far back in the pelvis as possible."—Ed.)

## STRESS INCONTINENCE IN WOMEN

R. E. VAN DUZEN

J. Urol., 55: 648-650, 1946

The author discusses the importance of stress incontinence as a urological problem. He states that in spite of the advances made in obstetrics in recent years, he sees more women with leakage of urine on coughing, sneezing, etc., than formerly. Stress incontinence may be seen in women with large uterine fibroids, some cases have been said to be due to spina bifida, and some to the

accidental inclusion of the fibres of the deep urethra in a stitch during cystocele repair. Rongy believes that excessive masturbation may cause incontinence, but the author considers that the congestion of the urethra associated with masturbation would be more likely to produce impediment to the flow of urine.

Many patients with stress incontinence are helped by local treatment to the urethra, such as urethral dilatation, instillations of weak silver nitrate solution, injection of sterile saline about the urethra, subcutaneous injection of thorium about the urethra, or pessaries. The benefit derived from estrogenic substances in these cases is doubtful.

In regard to surgical treatment, the author recommends a modification of the cystocele repair described by Royston and Rose. Two additional cotton or silk sutures are placed just anterior to the internal vesical sphincter including part of the bulbocavernosus muscle. The sphincter is localized by the bulb of a mushroom catheter drawn down against the internal urethral sphincter. The author tries to approximate the bulbocavernosus muscle so that the urethra is very snug about the catheter. The angle formed by the urethra with the bladder floor should approach a right angle.

Presacral neurectomy in the obstinate case may be very useful. In regard to this operation, although the textbooks describe a single nerve crossing the left iliac vessel just lateral to the bifurcation of the iliac, one soon learns to identify, in the living, many nerve fibres too small to recognize in the cadaver. Hoge and Jones recently described many types of arrangement of the nerve fibres between the ureters which cross either iliac vessel. When this is done, the delay in starting the act of urination is accomplished that many writers have denied.

(The subject of stress incontinence has been commented on in connection with several previous abstracts in the Survey (See February Survey, p. 134 and August Survey, p. 592). My experience has been that such simple local treatments as those mentioned by the author are not often helpful. The incontinence in some patients is only slight, being noted on severe muscular efforts, such as heavy lifting, coughing or hearty laughter, and not all patients consider themselves sufficiently inconvenienced as to want surgical relief. The procedure recommended by the author is no doubt effective in the type of case in which he employs it, although the Kennedy type of operation is more frequently applicable and usually successful. When the neck of the bladder is boggy, additional benefit will be derived from the employment of the Kelly type of vesical plication. I have had no experience with presacral neurectomy for this indication, and do not see just why it should be helpful.—Ed.)

## A CLINICAL AND PATHOLOGICAL STUDY OF THE POSTERIOR FEMALE URETHRA

R. L. DETER, G. T. CALDWELL AND A. I. FOLSOM

J. Urol., 55: 651-662, 1946

There exists a very meagre knowledge of the embryology of the female urethra, and at present the matter is not settled. In the present paper, the authors

list the findings as they have interpreted them, emphasizing the importance of the glandular structures encountered in the posterior female urethra and their significance in disease processes in this region.

Research by Korenchevsky (1935) indicates a definite homology between the prostatic urethra of the male and the posterior urethra of the female. He injected the diol of androsterone (CHO), a derivative of male sex hormone, into ovariectomized rats for 3 weeks in doses of 175 to 700 units a day. On dissecting the vagina and uterus of these rats, glands, not normally seen in the rat, were found in the vagina, at the base and in front of the bladder. These glands had the microscopic appearance of the ventral lobe of the male prostate. Thus, the name "female prostate gland" could be used instead of "female periurethral glands" in order to emphasize the homology of these glands in the male and female.

A brief study of the nature and occurrence of these glands in the posterior female urethra was undertaken. The study was confined to the proximal 1.5 to 2 cm. of the urethra. Periurethral glands were found to be present in 92 per cent of 100 urethras studied. It was found that the glands were distributed in the urethra approximately the same as in the male prostatic tissue. In regard to distribution along the length of the urethra, it was observed that the closer to the bladder the sections were taken, the greater was the number of glands seen. In 100 per cent of the specimens that were found to contain glands, these glands were found laterally. In 75 per cent they were found laterally and posteriorly. In 16 per cent they were found completely surrounding the urethra.

The authors emphasize the role played by the periurethral glands in harboring infection and distributing it to the upper urinary tract. The one symptom which points more directly to the female urethra than any other is bladder irritation with frequency. Folsom has presented the role of the posterior female urethra as a causative agent in the production of subjective symptoms of bladder irritation in cases where the rest of the urinary tract has been found normal. It is suggested that the pathological changes which take place in the posterior female urethra are produced by infection in the posterior urethral glands. The accessibility of the female urethra to contamination is not the only factor involved. Contaminating materials could easily be washed out as they reached the bladder if the urethra were a simple tube. But the glands in the posterior urethra provide ready receptacles to receive and distribute these materials to the upper urinary tract.

There is some foundation for the opinion that hormones play some part in the etiology of posterior female urethritis. In support of this is the observed frequency of urethritis at periods of life when there is the greatest possibility of hormone imbalance, particularly at or after the menopause when there is less estrogenic hormone present and the possibility exists for the largest amount of androgenic materials functioning in the female.

The pathological findings in this series of urethras are tabulated, and it is concluded that the number of glands in the posterior urethra, beyond a certain

point, is not a factor in harboring infection. A certain degree of glandular development seems to have a definite relationship to the development of posterior urethritis in females. 5 figures.

## URINARY INCONTINENCE DUE TO BILATERAL ECTOPIC URETERS

L. F. GREENE AND D. O. FERRIS

Surg., Gynec. & Obst., 82: 712-716, 1946

Urinary incontinence due to an ectopic ureteral orifice is not common. Among those cases reported, in most instances the condition was unilateral. The ectopic ureter is usually associated with complete duplication of the pelvis and ureter. In cases of bilateral ureteral extopia the orifices of the ectopic ureters are most frequently situated in the urethra or the vestibule of the vagina. The condition occurs with much greater frequency among women than among men, and in women the most outstanding symptom is urinary incontinence.

The diagnosis of bilateral ectopic ureters may be exceedingly difficult and, at times, may be only inferred. If the symptoms are suggestive, the urethra, vestibule and vagina must be carefully examined. The intravenous administration of indigocarmine is usually of little value. It may be possible to catheterize the ectopic ureters and to secure pyelograms. Excretory urography is valuable in the diagnosis of this condition. In most instances bilateral complete duplication of the renal pelves and ureters will be found.

The authors present 2 cases of bilateral ureteral ectopia. Both of these patients had been incontinent since birth. In each case bilateral heminephrectomy resulted in complete relief of the incontinence. From a study of these 2 cases it is observed that if incontinence persists after unilateral heminephrectomy, bilateral ureteral ectopia is suggested and further urologic investigation of the opposite kidney, including exploration, if necessary, is indicated. 7 figures.

(While this anomaly is extremely rare, and will probably not be encountered by most gynecologists, its possibility should certainly be thought of in cases of persistent urinary incontinence, associated with normal micturition, and dating back to infancy.—Ed.)

## OPERATIVE GYNECOLOGY

### CRITICAL STUDY OF 390 MAJOR GYNECOLOGICAL SURGICAL PROCEDURES

CHARLES M. MALONE

Am. J. Obst. & Gynec., 52: 291-298, 1946

The 390 major gynecological surgical procedures which are analyzed in this paper were performed at the Los Angeles County Hospital in 1943 and 1944. The average age of the patients was 34.4 years, and 66 per cent of the women were parous. The average preoperative stay was 8.9 days, and the average postoperative stay was 12.0 days. Sixty-three patients (16 per cent) had undergone previous pelvic surgery. Twenty-one of these had been sterilized previously by tubal ligation, and now presented symptoms requiring really adequate sterilization consisting of hysterectomy and bilateral salpingectomy. Thirty-one patients had further incomplete surgery consisting of unilateral salpingectomy and/or oophorectomy for inflammatory disease. Various writers have agreed that salpingitis is nearly always bilateral. The importance of complete surgery in pelvic inflammatory disease is stressed.

The subjective indications for surgery in this series were: pain and hemorrhage (individually or collectively), 81 per cent; tumor (pressure symptoms), 14 per cent; prolapse, 9.5 per cent; and miscellaneous, about 10 per cent. Objectively, pelvic inflammatory disease was the principal diagnosis in 43 per cent of the patients; fibromyomata uteri, with and without inflammatory disease, 38 per cent; and uterine hemorrhage, shock, acute pelvic pain, etc., 19 per cent. A correct preoperative diagnosis was made in 69 per cent of the patients, a partially correct diagnosis in 16 per cent, and an erroneous diagnosis in 15 per cent.

The various types of surgical procedure carried out were: subtotal hysterectomy, 14.1 per cent; subtotal hysterectomy plus, 57.7 per cent; total abdominal hysterectomy, 10.0 per cent; total abdominal hysterectomy plus, 1.5 per cent; vaginal hysterectomy, 5.0 per cent; adnexal surgery, 8.0 per cent; and miscellaneous, 3.8 per cent. The relative infrequency of total abdominal and vaginal hysterectomy is explained by the presence of advanced stages of pathologic disease particularly pelvic inflammatory disease, which would make the total operation more difficult and dangerous. Spinal anesthesia was employed in 79 per cent of the cases, cyclopropane in 12 per cent, and ether, curare and miscellaneous in 9 per cent. There were no deaths or unusually severe accidents attributed to the anesthetic agent.

The total morbidity was 20 per cent. The most essential preoperative factors in reducing morbidity were found to be cauterization of the cervix, and normal urine and blood findings. An absolutely afebrile period of at least one week before surgery, particularly in pelvic inflammatory disease, is important. In

60.4 per cent of the series an appendectomy was done; this slightly raised the morbidity. Complete and careful evaluation of kidney function must be carried out in patients undergoing vaginal plastic procedures.

There were 4 operative deaths, a mortality incidence of 1.03 per cent. In none of these patients were the operative criteria enumerated by Polak and Tollefson fulfilled.

In conclusion, particular stress is placed upon "incomplete surgery". It is desired that complete and adequate surgery be done if the abdomen is opened at all.

(In this statistical paper, the author's chief insistence is upon "complete surgery" in pelvic inflammatory disease, but it seems to me that such statements need qualification. If he means that both tubes should be removed when both are diseased, and that hysterectomy is also advisable when the uterus is extensively involved in adhesions to surrounding viscera, there will not be much difference of opinion. If, on the other hand, he would insist on routine removal of the uterus, even though it seems normal, whenever bilateral salpingectomy is necessary, there will be differences of opinion.

In a recent visit to Los Angeles, I found that many excellent gynecologists there do actually follow this plan, explaining that retention of the uterus is commonly later followed by excessive bleeding. This was rather surprising to me, as it did not correspond with my own experience. We can talk all we please about the unimportance of menstruation, but the fact remains that many young women do feel somewhat defeminized if the function is abolished, and that its conservation does have a genuine psychological advantage. Why retention of a healthy uterus and normal ovaries should make the patient abnormally prone to subsequent bleeding after simple removal of the diseased tubes is not clear, though there is certainly no reason why such a uterus might not at times later become the source of functional bleeding, just as in a woman who has never had pelvic inflammatory disease.

One must of course individualize on the basis of pelvic operative findings, but certainly there are cases in which the possible future prophylactic value of routine hysterectomy would be more than counterbalanced by the unhappiness which such a plan might later inflict upon many patients, especially those of the younger group.—Ed.)

## TOTAL ABDOMINAL HYSTERECTOMY; A STUDY OF 500 CASES

W. C. DANFORTH

Am. J. Obst. & Gynec., 52: 218-227, 1946

The author points out the advantages of removal of the cervix in hysterectomy operations. Although the number of women in whom cervical cancer develops after the subtotal operation is small (an incidence of 2 per cent has been given), the risk is worthy of notice. A second reason for elimination of the cervix is that many cervixes are unhealthy and may produce troublesome symptoms after subtotal operation. For these reasons the author considers removal of the cervix highly desirable provided it may be accomplished without mortality increase, or at least with an increase no greater than the number of cases of stump cancer would account for. The purpose of the present paper is to indicate what may be done by the total operation in the hands of trained men.

The 500 cases of total abdominal hysterectomy considered in this presentation were performed between the latter part of 1939 and August, 1945. The indication for operation in 319 cases was myoma. Adenomyosis as the principal indication was found in 52 cases. Functional bleeding called for treatment in 53 cases. Carcinoma of the corpus was found 27 times. Sarcoma of the uterus occurred once. Endometriosis was the primary indication 35 times. In 70 cases the condition of the cervix caused a note to be made by either the pathologist or the operator. Cases of simple erosion of moderate degree are excluded from this figure.

In the present series there were 2 deaths, an incidence of 0.4 per cent. In another series of 744 subtotal hysterectomies, there was a mortality of 0.66 per cent. Obviously the danger is not increased under proper conditions. However, without a thorough familiarity with pelvic anatomy and technique, there is definitely greater danger with the total operation. According to the rule of the American College of Surgeons, 141 patients, or 28.2 per cent, had a morbid recovery, but serious morbidity was exceptional. Thrombophlebitis occurred 3 times, and ureteral injury occurred twice. Both of the latter 2 cases recovered, although nephrectomy was required. The bladder was opened 4 times; all of these recovered without trouble. One of the deaths was caused by septicemia, a tracheobronchitis also being found at autopsy. The other death was from uremia with failure of urinary secretion; the absence of ureteral obstruction was proved.

In 239 cases the adnexa were not disturbed on either side, while in 136 cases the ovary and tube, or at least the ovary, were left on one side. Conservatism in this regard is obviously advantageous; however, an unhealthy ovary is better removed.

Operative technique is discussed, and it is pointed out that, if division of the vaginal wall is made close to the cervix, the vagina need not be shortened. It is important, whether the total or subtotal operation be done, that the ovaries be left freely movable and with good blood supply.

It is the author's experience that, in trained hands, total abdominal hysterectomy may be used frequently or even almost routinely. Its advantages are sufficient to warrant such frequent use. 5 figures.

(No question was more widely or more sharply discussed than that of total vs. subtotal hysterectomy, but the controversy has drawn pretty well to a close, with the total hysterectomists in command of the field, in so far as the preferential policy is concerned. There are few gynecologists, however, who do not recognize that even in the hands of the most expert operators it would be silly to insist on the ideal total procedure in the presence of conditions which clearly make the hazard greater than that involved in the retention of even a pathological cervix. The total procedure is often about as simple as the subtotal, but I do not see how anyone can maintain that this is the rule, and that the total operation does not require more care and skill and involve a slightly greater hazard than the subtotal, in spite of at least some figures to the contrary. In the hands of the occasional total hysterectomist there will be little difference of opinion on this point. In general, the total operation is clearly the method to be preferred except when contraindicated by the general or local pelvic conditions, or by the personal limitations of the surgeon.

I agree with Danforth that there is little force to the objection which many have urged

against the total operation, that the vagina is shortened, with consequent dyspareunia. I do believe that there is occasional complaint of dyspareunia, at least for a time, but I have always felt that this is to be explained, not by shortening of the vagina, but by the tenderness of the scar in the vaginal vault.—Ed.)

## BLEEDING FROM THE CERVIX AFTER SUBTOTAL HYSTERECTOMY

J. E. DAVIS AND D. B. CHEEK

J. A. M. A., 131: 816, 1946

From January 1, 1938 to July 1, 1945, 87 patients have presented themselves at the authors' clinic with bleeding from the cervical stump. Of this group, 40 patients, or 46 per cent, were found to have carcinoma of the residual cervix. Of these 40 there were 6, or 15 per cent, who had a benign appearing cervix at the time they were first seen with the complaint of bleeding. It is clear, from this small group of cases, that the only sure way to detect early carcinoma after a subtotal hysterectomy is to view with alarm any bleeding which occurs. The authors state that, regardless of a history suggesting the presence of menstruating endometrium, regardless of the appearance of the cervix and regardless of estrogen therapy, every patient who has vaginal bleeding at any time after a subtotal hysterectomy deserves a biopsy of the cervix and a gentle curettage of the cervical canal.

The impression in this group of 87 cases is that the incidence of cancer is not appreciably altered by the presence or absence of ovaries. Of 56 patients with one or both ovaries remaining, 22 had cervical cancer. Of 16 patients with both ovaries absent, 8 had cervical cancer. In 15 patients the details were not known; of these, 10 had cervical cancer.

It seems plausible to conclude that many subtotal hysterectomies are performed in the presence of an early carcinoma of the cervix. Since March, 1944, it has been the policy in the authors' gynecologic dispensary to make a routine biopsy of the cervix on each patient on whom a major gynecologic procedure was planned. During the period included in this study carcinomas were found in 9 cervices that did not present suggestive indications.

(This is an interesting study, and the serious significance of bleeding from the cervical stump is emphasized by the fact that nearly one half of the authors' group of such cases were found to have carcinoma. Every gynecologist whose experience goes back to the not far distant days when the prevalent technic of hysterectomy was by the supravaginal method has had the unpleasant experience of having patients return with bleeding from the cervix, with frequently the finding of a cancer which was undetected at the time of operation or which developed later. Such experiences as this, not to speak of the patients left with troublesome cervical leucorrhea, explain why total hysterectomy has established itself as the technic of choice. There will be general agreement with the authors' injunction that careful inspection, biopsy and curettage of the canal is indicated in all cases of bleeding from the residual cervical stump.—Ed.)

## THE MANCHESTER OPERATION, WITH SPECIAL REFERENCE TO PARTURITION AND COMPLETE PROLAPSE; A REPORT OF 206 CASES

CHARLES A. GORDON

*Am. J. Obst. & Gynec.*, 52: 228-236, 1946

During the 10-year period from 1934 to 1943, 236 women were operated upon for prolapse of the uterus at the author's hospital. The types of operation were as follows: Manchester, 206 cases; Le Fort 2 cases; vaginal hysterectomy, 21 cases; and interposition, 7 cases. The end results in many of these cases have been studied in order to discover whether the Manchester operation has a place in the management of prolapse of the uterus during the reproductive period, and whether or not it is effective in the correction of complete prolapse.

In this series of 206 Manchester operations there were 36 women less than 40 years of age, 16 of whom were less than 35 years old. Parturition is known to have occurred subsequently in 10 cases. In 5 of these no details of labor or actual end results are known, except in one case where prolapse recurred. The essential clinical data in the other 5 cases is summarized below. In none of these did prolapse recur.

Case I.—Aged 26 years. Cervix not amputated. Five years later, 10 hours of labor with 9-pound baby; low forceps and episiotomy.

Case II.—Aged 34 years. Cervix not amputated. Four years later, 5 hours of labor with 8-pound baby; episiotomy.

Case III.—Aged 32 years. Cervix amputated. Three years later, 15 hours of labor with 10-pound, 3-ounce baby; manual rotation of right occipito-posterior, low forceps and episiotomy.

Case IV.—Aged 34 years. Cervix amputated. One year later, 3 hours of labor with 10-pound, 7-ounce baby; low forceps and episiotomy.

Case V.—Aged 32 years. Cervix amputated. Three years later, 12 hours of labor with 5-pound, 5-ounce baby; lower segment cesarean section for rigid cervix.

Rawls and Hunter have shown that there is a very definite risk in pregnancy and labor following amputation of the cervix. Should abortion occur, as it frequently does, there is increased liability to retention of placental tissue and sepsis. In labor, partial or complete failure of cervical dilatation may occur, even uterine rupture. Whether part of the combined operation or the Manchester, cervical amputation is not a good operation for women in the reproductive period.

The author discusses the relative merits of the combined operative procedure and the Manchester operation for correction of uterine prolapse during the reproductive period of life. The Manchester operation is recommended. All of the cases of parturition subsequent to the Manchester operation which the author has been able to find are reported in Table I. The Halban operation is included because it differs little from the Manchester procedure.

Whether the Manchester operation is suitable for women in the reproductive period is a question of importance since its alternative, the combined operation, is unsatisfactory. Operations for correction of uterine prolapse are usually performed after the menopause, and comparatively few cases of subsequent pregnancy have been reported. Some gynecologists remain unconvinced that women may be carried safely through parturition without severe dystocia or serious damage to the plastic end result. Yet many who have performed this operation on young women have reported no serious dystocia or any pathology in the puerperium. The incidence of forceps deliveries may be discounted, since instrumental delivery through a wide episiotomy is advisable after any vaginal plastic procedure. The possibility of cesarean section, though remote, must be

TABLE I  
*Parturition subsequent to the Manchester operation*

	OPERATION		NO. IN CHILD- BEARING AGE	NO. OF DE- LIVERIES	SUB- SEQUENT RE- CURRENCE	OPERATIVE DELIVERY
	Man- chester	Halban				
Maier and Thudium...	138		47	13	None	Instrument 3
Shaw.....	664			30	5	None
Gordon.....	358		58	18	1	Instrument 8, Cesa- rean section, 1
Hunter.....	19		19	1	None	None
Fothergill*	156			32	1	Instrument 23
Leventhal and Boshes..	51			1	None	None
Salmon.....	254			2	None	None
Herzfeld and Tod.....	132			11	None	Instrument 3
Williams.....	45		45	27	None	None
Bazan and Althabe....	354			8	None	Instrument 1
Borras.....	145	293		4	None	None
Mestitz.....		†		†	None	None
Schmid.....		605		4	None	None
Lacey.....	521		382	89	33	Instrument 35

\* Included in Lacey's figures.

† Large series.

considered, particularly if the cervix has been amputated. Even complete prolapse of the uterus may be corrected without this dangerous procedure.

The Manchester operation has given excellent results in 62 cases of complete prolapse in which observation has continued for long periods of time.

(While the Manchester operation has achieved wide employment in this and other countries, there has been hesitancy in many clinics in employing it on patients in the reproductive period of life without sterilization at the same time. As the author states, the plan of combining simple types of plastic repair with abdominal suspension has been more or less a makeshift, and not a very satisfactory one. Gordon has done a service in collecting the reports of all cases in which parturition has followed the performance of the Manchester operation (Table I), showing not only that recurrence is relatively uncommon, but, even more interestingly, that there is little hazard of obstetrical complications.

While it is a wise plan to defer major plastic procedures until after the menopause, if possible, this cannot always be done, and such procedures must at times be resorted to

when subsequent pregnancy is possible and often strongly desired by the patient. It must also be remembered that simple median approximation of the cardinal ligaments does not suffice to correct the cystocele which is so often associated with prolapse, so that some form of bladder advancement operation must be combined with the cardinal ligament procedure. The complete interposition operation of Watkins is, I believe, always contraindicated, but my experience has been that there is no unfavorable effect produced on subsequent labors by the advancement operations, and this is also indicated by Gordon's collective review of reported cases.

As to amputation of the cervix, most gynecologists will agree that this carries with it such hazard as to contraindicate it, in spite of the fact that no very serious results occurred in the 3 cases in Gordon's own group. The chief hazards are those enumerated by the author himself. In many, perhaps most cases of prolapse, amputation of the cervix is indicated because of hypertrophy, chronic cervicitis or other pathology, and under such circumstances should be done. But not during the reproductive era, when cervical pathology should be handled as well as possible with more conservative measures, such as electrocauterization or tracheloplasty.—Ed.)

## INDWELLING CATHETER VS. INTERMITTENT CATHETERIZATION

E. S. HICKS

Canad. M. A. J., 55: 69-70, 1946

The author states that the harmful effect of the indwelling catheter is one of the legends that has been handed down in surgical practice, and presents data which prove that it is a sensible and practical procedure, reducing the morbidity from 18 to 3 per cent.

The present conclusions are based on records of 2000 cases, largely female. The type of catheter preferred is a 12 to 16 French winged catheter. Whatever the type, it must be soft enough to collapse easily so that there will be no pain upon its removal. The usual preoperative catheterization is omitted, and at the conclusion of the vaginal part of the operation the indwelling catheter is inserted under perfect vision and without trauma, since the urethra is relaxed. The catheter is fastened without tension with 2 strips of adhesive, one near the labia and one on the upper part of the thigh. Ordinarily the catheter is removed by the morning of the third postoperative day. From practical experience in vaginal hysterectomies, vesico-vaginal fistulae, etc., the author knows that these small catheters can be left in much longer with impunity.

By this method only one catheterization occurs, and it is properly done. The bladder is empty and remains empty for the abdominal part of the operation. An empty bladder tends to avoid injury to the bladder in anyone's hands. As all tension is removed, the bladder can heal quickly if accidentally injured. Abdominal distention is avoided. The author finds the method useful in operations for hernia. No sulfa drugs or penicillin were used in any of the patients included in this series. They may be helpful in a patient with preoperative urinary infection. Drugs are not the answer to this trouble, and no antiseptic will render residual urine aseptic.

(There are differences of opinion and practice among gynecologists as to the advisability or inadvisability of employing indwelling catheters postoperatively, and with this question, as with so many postoperative details, it is probably wise to avoid inflexible routines. I see no advantage, and some disadvantage, in the use of the retention catheter after most abdominal operations, in spite of the relative frequency of urinary retention. The latter, however, should be guarded against by watchful nursing care rather than by the routine use of indwelling catheters. Nurses should be impressed with the fact that catheterization with reasonably aseptic care is far less of a menace to the patient than the occurrence of overdistention of the bladder, with its characteristic sequence of persisting residual urine and cystitis. It is the atonic bladder, with residual urine, that is so highly prone to infection. Should retention occur, catheterization after voiding should be kept up until the bladder has regained its tone.

With vaginal operations, especially the extensive plastic procedures, I believe that an indwelling catheter for the first few days serves a useful purpose, although I do not think it as completely free of risk of cystitis as does the author of the paper. In these cases, however, postoperative retention is very common, and catheterization may be much more difficult for the nurse because of the retraction of the urethra entailed by many operations on the anterior vaginal segment. The daily injection of such antiseptics as mercurochrome may give additional protection, and in addition I have been using prophylactic sulfa therapy in moderate dosage. While in most cases a mushroom type of catheter is less apt to slip out and is probably not disadvantageous otherwise, I more often use a plain catheter, because it seems to involve less trauma on withdrawal. I am aware, however, that there are differences of opinion on this point, as on others which I have mentioned. The care of the bladder is apt to be the *bête noir* in the postoperative care of plastic cases, and the conscientious surgeon is not likely to throw the entire burden of responsibility for this on his subordinates.—Ed.)

## STERILITY

### THE PROBLEM OF STERILITY TODAY

M. E. DAVIS

Am. Practitioner, 1: 1-14, 1946

In approaching the sterility problem today, a knowledge of the anatomy and physiology of the reproductive organs leads to a careful organic and functional survey of the reproductive function by all the methods at our disposal. This rational approach has improved the prognosis of the sterile couple tremendously. The author begins this paper with a discussion of the anatomy and physiology of the reproductive system.

The vagina, uterus and fallopian tube must maintain an unbroken continuity of lumen for conception to take place. The ovary must produce mature follicles at periodic intervals, and these follicles must discharge their ova in the proximity of the ostium of the tube to facilitate entrance into the tube. The normal tube undergoes contractions and the cilia on the mucosal epithelium produce currents by which the ovum moves downward through the lumen toward the uterus. Spermatozoa move upward by their own efforts through the uterine cavity and into the tube where they meet the ovum and one fertilizes it. The fertilized ovum must then be transported into the uterine cavity for implantation. Many abnormal factors can enter into this process, causing decreased fertility or sterility. Ovarian function with the periodic development of mature follicles and rupture of these follicles is dependent on the normal function of the anterior lobe of the pituitary. Successful implantation of the fertilized ovum depends on the normal secretion of estrogen and the hormone of the corpus luteum to prepare the endometrium.

In examining the sterile couple, physical soundness must be evaluated. Inflammation of the reproductive tract is the most common disorder resulting in sterility. Infection, congenital malformations and tumors may interfere with normal patency of the reproductive tract. Abnormal position of the pelvic organs may decrease the ease of entrance of spermatozoa into the cervical canal. Careful pelvic examination should be carried out with all of these points in mind. The cervix should be examined with a speculum so that the external os may be visualized and the physical character of cervical secretions determined.

Organs which are apparently normal on pelvic examination must be studied further by visualization of the reproductive tract using an opaque oily medium which is injected slowly into the uterine cavity under fluoroscopic control. Stereoscopic films are then taken and repeated in 24 hours. Varying degrees of lack of normal fusion of the uterus are a not uncommon finding, occurring in almost 10 per cent of the author's series. Closure of the tubes may be recognized by this method and the point of occlusion, which may be very important from a prognostic viewpoint, may be noted.

The male should be evaluated from the anatomic standpoint and any abnormalities of the urethra, epididymis, testicle, prostate and seminal vesicles should be correlated with the subsequent investigation.

In evaluating function of the reproductive organs, a careful resume of the menstrual history is the first clue to ovarian function. However, normal menses are not proof of normal ovulation. The endometrium provides a convenient and accessible means of determining ovarian activity. The endometrium before ovulation has taken place shows a typical microscopic appearance. This picture is characterized by the presence of long, straight and only slightly curved glands lined by a layer of cells in which the nuclei are basally situated, and in which there is no evidence of secretory activity. The stroma is relatively thick and shows deeply staining small cells. This phase is due to estrogen and is evidence of ovarian follicular activity. When ovulation has occurred, the corpus luteum forms and progesterin is secreted. In the endometrium the glands become markedly tortuous. The secretion-distended gland cells, with centrally placed nuclei, give a tufted appearance to the lumen of the glands. Stroma is less dense and contains larger pale staining cells and evidence of increasing congestion. Biopsy specimens taken in the days preceding menstruation exhibit this picture as evidence that ovulation has occurred and a corpus luteum formed.

The most recent observation in the study of reproductive physiology is the relationship of body temperature and ovarian activity. Follicle rupture and corpus luteum development raise the level of the basal temperature during the latter half of the cycle. Basal temperature graphs are reliable indices in at least 3 out of 4 women. In the remaining 25 per cent the curve is so atypical that accurate interpretations cannot be made.

Often the basal metabolic rate determination is of value. The majority of the author's patients had a basal metabolic rate within normal limits; 26.6 per cent were below the accepted lower limit of normal (less than  $-10$ ). Thyroid medication increases the chances of conception in this group. The metabolic rate should also be determined in the male.

The next step in evaluation of the sterile couple is examination of the male ejaculate. Number, normalcy and activity of spermatozoa are determined. The presence of a large number of abnormal forms is noted. A post-coital examination, or Huhner's test, permits the determination of the effect of vaginal secretions on the spermatozoa.

A complete and detailed history of each of the partners is important. This should include general constitutional diseases, operations, onset and character of puberty and any possible genital infections. The use and type of contraceptives should be determined. Coital habits, particularly in regard to frequency and time interval in the ovarian cycle, should be investigated. A history of previous obstetric episodes—abortions and delivery complications—should be obtained. Each partner should then have a careful general physical and local examination.

The patency of the female reproductive tract must definitely be determined. This may be accomplished by the Rubin test or by the injection into the reproductive tract of iodized oil under fluoroscopic control. It has been the author's practice to perform the Rubin test and to follow it immediately with hystero-

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Organs which are apparently normal on pelvic examination must be studied further by visualization of the reproductive tract using an opaque oily medium which is injected slowly into the uterine cavity under fluoroscopic control. Stereoscopic films are then taken and repeated in 24 hours. Varying degrees of lack of normal fusion of the uterus are a not uncommon finding, occurring in almost 10 per cent of the author's series. Closure of the tubes may be recognized by this method and the point of occlusion, which may be very important from a prognostic viewpoint, may be noted.

far as the extent of tubal involvement is concerned. Davis' finding of a 10 per cent incidence of fusion defects in his group of cases seems too high, and certainly it is much higher than in my own experience.

Again, there are differing degrees of enthusiasm as regards basal temperature recordings. I personally see no advantage in this diagnostic method in women with reasonably regular periods, in whom simple menstrual or premenstrual biopsy has shown the cycles to be characteristically ovulatory. In such women all the temperature curves that have ever been made have confirmed what has long been known as to the usual ovulation span. Knowing this, gynecologists have always advised coitus especially at this optimum phase, and this is just as likely to accomplish the same purpose without basal temperature recordings, aside from limitations and possible errors in the latter. In women with very irregular cycles, on the other hand, the rationale of temperature recordings is on a sounder footing. Finally, I wonder if we could demonstrate statistically or otherwise that a woman with bilateral patency has twice as much chance of conceiving as the woman with only one patent tube.—Ed.)

## TESTICULAR DYSFUNCTION: DIAGNOSIS AND TREATMENT

ALBERT SEGALOFF

Am. Practitioner, 1: 15-22, 1946

The author presents a brief discussion of the physiology of the testis. The production of motile, fertile, adequately mature spermatozoa in adequate numbers is brought about by the interplay of the testis and pituitary. There are 2 basic types of failure of this function: the pituitary can fail to produce its gonadotropic hormones or the testis can fail to respond to stimulation from the pituitary. The 6 basic types of testicular failure are outlined in Figure 2. The author presents case reports which illustrate these various types of failure.

In studying patients with testicular dysfunction it is of great importance to obtain a careful history. The patient's age and occupation should be noted, and whether he has been exposed to radiation or toxic materials. Has the patient ever reached puberty, and if so, at what age? Has he ever had orchitis, epididymitis or other genito-urinary infections? If he is cryptorchid, do the testes ever descend into the scrotum? Has he undergone any surgical procedures, particularly repair of inguinal hernia? The psychosomatic features should be evaluated. Postpubertal testicular failure is followed by a train of symptoms similar to menopausal symptoms in women.

A complete physical examination should be done, noting the patient's size and proportions. The distribution of body hair should be noted. Voice pitch should be noted, and the larynx palpated for its normal masculine development. The presence or absence of gynecomastia should be noted. In examining the genitalia the size of the penis and scrotum and the size and consistency of the testes are important. If the testes are not normally located in the scrotum it is well to ascertain if they will descend by placing the patient in a warm environment. The ducti deferens and the epididymi should be palpated for possible blocking lesions.

salpingography. In the Rubin test the pressure of gas should never be allowed to exceed 200 mm. of mercury. Neither test should be performed in the presence of acute inflammatory disease or subsequent to ovulation, as there is then the possibility of an existing pregnancy.

Regardless of abnormal findings in the previous examinations, the remainder of the study should be carried out for a complete and intelligent evaluation of all factors. The male should be examined as previously outlined. The investigation is completed by study of the endocrine factors which may be involved.

In regard to treatment, the first attempt is the restoration of the genital tract to an anatomic normal. Malpositions of the uterus should be corrected and lower genital tract infection should be eradicated. Any barriers to patency of the reproductive tract should be removed where the function of the organs may be preserved. The Rubin test or injection of iodized oil may serve effectively to break adhesions. The couple should be advised concerning the optimum time for intercourse, and should be cautioned against too frequent attempts. Those individuals with basal metabolic rates below zero should be given thyroid. The general physical condition of the couple should be raised to the optimum. Gonadotropic hormones for the relief of sterility have not yielded satisfactory results. In those cases where the wife is completely normal and the husband has a complete absence of spermatozoa or so few spermatozoa that conception is unlikely, artificial insemination may be considered.

The first step in a program for sterility prevention is education of the people to a realization of the importance of the problem. The premarital examination affords one opportunity for such education. Another factor in preventing sterility is conservatism in treatment of genital infections. Lower genital tract infections should be treated adequately to prevent ascension of infection, and in all gynecological surgery on women in the childbearing age, conservation of ovarian function and preservation of patency of the reproductive tract should be the constant attempt of the operator.

Of 567 patients registered in the author's sterility clinic between July, 1931, and December, 1942, who have been followed for at least one year, 202, or 35.6 per cent, conceived and 169 had living children. The shorter the period of infertility, the greater were the chances of conception. A lack of tubal patency was the most common cause of sterility, bilateral tubal closure being found in 190, or 22 per cent, of 869 women examined. Ten of this group conceived. The woman with bilateral patency has about twice as much chance of conceiving as the woman with only one patent tube. 20 figures.

(This is a systematic and comprehensive review of the subject. The views expressed are sound, although gynecologists will naturally differ in their evaluation of the many possible factors in sterility, and in the relative importance which they attach to various diagnostic procedures. Some, like myself, prefer tubal insufflation to hysterosalpingography for routine use, although recognizing that there is a place for both methods. Others believe that hysterosalpingography should be a part of the study in every case, its chief advantage being that it reveals the point of occlusion of the tubes. However, if the tube is definitely closed at any point, the prognosis is likely to be poor enough regardless of the type of plastic operation that is done, and surprises at operation are not infrequent in so

by pituitary failure, which is required for the proper diagnosis of Fröhlich's syndrome.

Treatment of testicular failure is none too satisfactory. It may consist of attempts to make the testis produce its secretions (stimulation therapy) or substitution for the testicular secretion. Cases with failure of the anterior lobe of the pituitary are suited for stimulation therapy. Chorionic gonadotropin of human pregnancy urine stimulates production of testosterone by the interstitial cells of Leydig if given in sufficient doses. Pituitary extracts with follicle-stimulating activity are available but are usually of low potency. Pregnant mare's serum should be used in sufficiently large doses with periods of rest, since anti-hormones are rapidly formed against it. It is generally agreed that there is no effective therapy at present for advanced spermatogenic failure of any type.

Substitution therapy consists in the administration of testosterone or one of its derivatives. Parenteral therapy with testosterone propionate is probably the most useful. 9 figures.

(Until very recent years many gynecologists were discouraged at the lack of interest displayed by our genito-urinary confrères in the study of the male sterility problem. While this criticism is still a very valid one in many individual instances, there are now many urologists who have become intensely interested in the problem, and who no longer assure a man, as did some of their predecessors, that he is capable of fertilizing his wife simply because some live spermatozoa can be demonstrated in the seminal exudate squeezed out by prostatic massage. Many gynecologists, therefore, prefer to leave the entire study of the male partner to their urological colleagues, and to this plan there can be no valid objection.

On the other hand, there are some advantages to the gynecologist, properly trained in such procedures, in making the initial examination of the semen himself, or even in a general evaluation of the husband from such broad standpoints as, for example, thyroid function. Certainly he would not wish to treat the male patient should any seminal or endocrine deficiency be revealed. The problem of sterility is a joint one between husband and wife, and their roles cannot be too sharply disassociated. I believe I am correct in saying that the American Board of Gynecology and Obstetrics does not consider that such limited evaluation of the husband is any infringement of its requirement that gynecologists are expected to restrict their practice to female patients.—Ed.)

Semen specimens for analysis should be collected by coitus interruptus or by manual manipulation into a clean dry test tube, and not collected in a condom. In a specimen with normal motility of the highest order, 80 to 95 per cent of the cells are actively motile. Counts require only a few easily prepared reagents and the usual blood counting apparatus. The diagnosis of abnormal sperm count and motility should be made only after repeated examinations obtained after at least 72 hours of sexual abstinence. If no sperm are present, it must be ascer-

FIG. 2  
*Characteristic findings in testicular dysfunction*

	URINE		SPERM*		SECONDARY SEXUAL CHARACTER- ISTICS	TESTICULAR BIOPSY	
	17-Keto-steroids	Gonad-stimulating hormone	Count	Motility		Tubules	Leydig cells
Normal	→	→	→	→	→	→	→
Combined testicular failure	↓	↑	○	○	↓*	Sclerotic	Atrophic
Spermatogenic failure	→	↑	○	○	→	Sclerotic	→
Leydig cell failure	↓	↑	→ ↓	○	↓*	Spermato-genesis usually depressed	Atrophic
Combined pituitary failure	↓†	↓	○	○	↓*	Atrophic	Atrophic
Follicle-stimulating hormone failure	→	↓	○	○	→	Atrophic	→
Luteinizing hormone failure	↓†	→ ↓	→ ↓	○	↓*	→	Atrophic

\* Depends on age at onset.

† In these types 1000 I.U. daily of chorionic gonadotropic hormone will produce a rise in the 17-ketosteroid excretion.

→ Normal. ↑ Increased. ↓ Decreased.

tained whether the testis is not producing sperm or whether the sperm fail to reach the ejaculate. This is accomplished by testicular biopsy and cytologic examination of the specimen.

Frölich's syndrome is often diagnosed incorrectly in fat boys whose genitals are obscured by the huge fat mass, or in prepubertal fat boys. When hypogonadism does occur in these boys it is usually accompanied by an increased titer of urinary gonad-stimulating hormone and, therefore, could not be caused

by pituitary failure, which is required for the proper diagnosis of Fröhlich's syndrome.

Treatment of testicular failure is none too satisfactory. It may consist of attempts to make the testis produce its secretions (stimulation therapy) or substitution for the testicular secretion. Cases with failure of the anterior lobe of the pituitary are suited for stimulation therapy. Chorionic gonadotropin of human pregnancy urine stimulates production of testosterone by the interstitial cells of Leydig if given in sufficient doses. Pituitary extracts with follicle-stimulating activity are available but are usually of low potency. Pregnant mare's serum should be used in sufficiently large doses with periods of rest, since anti-hormones are rapidly formed against it. It is generally agreed that there is no effective therapy at present for advanced spermatogenic failure of any type.

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## MISCELLANEOUS

### ENTEROUTERINE FISTULA; WITH A REVIEW OF THE LITERATURE AND REPORT OF AN UNUSUAL CASE

S. Z. HAWKES

*Am. J. Obst. & Gynec.*, 52: 150-153, 1946

In 1933 Danforth and Case collected 58 cases of fistulous openings between the bowel and the uterus in the past 200 years, and since then 20 additional cases have been reported. Possible causes are: (1) traumatic or spontaneous rupture of the gravid uterus with a loop of intestine entering the tear; (2) peritonitis with abscess formation—abscess rupturing into bowel and uterus simultaneously; (3) carcinoma, usually of uterine body, when malignant tissue undergoes ulceration and necrosis with development of fistula between it and loop of bowel which becomes adherent; (4) puncture of uterine wall with concomitant injury of bowel during uterine curettement. Of the reported cases permitting analysis, in 18 the fistulous tract was between the small intestine and the uterus, and in 17 between the large bowel and uterus. In 3 cases both the large and small bowel were involved. As to treatment, Crossen and Crossen feel that the condition is best handled by abdominal section with mobilization and separate closure of the bowel wall.

The author presents the case of a 22 year old woman, married, with one child, who complained of severe abdominal pains, especially in the left lower quadrant, with fever and malaise. A pelvic mass was noted on the left side by a local physician, and a few days later the patient began to pass feces through the vagina. Since this occurred she had had no bowel movements through the rectum. Her menstrual periods had been regular, she did not believe herself pregnant and denied instrumentation.

A diagnosis of enterouterine fistula was made; the fistulous tract between bowel and uterus was proved by instilling water into the rectum and observing its return through the cervix. Blood, intravenous fluids and nutritional supplements were administered prior to drainage of the mass through a left lower quadrant muscle-splitting incision. Bowel movements through the rectum were resumed 2 weeks after drainage of the abscess, but there continued to be occasional temperature elevations and palpable enlargement of the left-sided mass.

Therapy for the next several months consisted of frequent transfusions, vitamin supplements and a high caloric diet. When the fistula did not heal spontaneously, a Devine transverse colostomy was performed, followed somewhat later by laparotomy to repair the fistulous tract. A portion of the sigmoid colon was found to be involved with the left adnexal mass. The bowel was freed, the cicatrized portion being excised and an end-to-end anastomosis performed. The tubo-ovarian mass was removed. Pathologic report of tissue removed showed chronic suppurative salpingitis and abscess formation of the left ovary. A

barium enema 3 weeks after operation showed colonic continuity well re-established; the spur of the transverse colostomy was crushed, and the bowel mucosa dissected free from the skin and inverted to allow closure of the skin.

It is believed that this patient had a chronic salpingitis with a cystic ovary on the left side. The ovarian cyst became inflamed with the formation of an abscess which ruptured into the uterine cavity and into the bowel. The point of rupture into the uterus must have been through the lumen of the tube.

(Cancer of the uterine corpus does not cause enterouterine fistula nearly as often as advanced cervical cancer produces rectovaginal fistula, but in rare cases this complication may occur. Such fistulas will not heal spontaneously, and their correction is difficult and sometimes impossible, so that it may be necessary to deflect the fecal current by establishing an artificial anus. The fistulas brought about by trauma or by the rupture of abscesses into the uterus, if not large, may close spontaneously. When closure is necessary, the results are usually good, the abdominal route being about the only feasible one if the fistula involves the corpus. Sometimes the operation is comparatively simple, but often it is difficult.

Some years ago I operated upon a woman of about 62 who had what was thought to be an infected left ovarian cyst, and who for many days had shown a septic temperature curve. The supposed cyst was found to be a huge pyometra about the size of a 3 months gestation, and brought about by the rupture into the uterus of a sigmoid diverticulitis. The uterus was removed after clamping off the cervical canal to avoid leakage of pus, and the patient recovered.

I recall reading an account many years ago of the autopsy of a patient who had died following criminal abortion. The postmortem showed that the abortionist's curette had perforated the uterine wall and then the sigmoid. My recollection is that the bowel was more thoroughly curetted than the uterus. In another patient whom I saw a hook-like instrument used by the abortionist had perforated the uterus and caught an intestinal loop, cutting it across and drawing the proximal bowel into the uterine cavity, which was filled with fecal material and pus.—Ed.)

## ABDOMINAL WALL FIBROMA (URACHAL?) SIMULATING OVARIAN CYSTOMA

C. E. McLENNAN AND E. G. HOLMSTROM

*Am. J. Obst. & Gynec.*, 52: 154-156, 1946

A lower abdominal mass in a 50 year old woman was first mistaken for a pregnant uterus, later assumed to be an ovarian cystoma, and finally, at operation, demonstrated to be a degenerating fibroma of the anterior abdominal wall. This case is interesting both because of the difficulty in diagnosis and the comparative rarity of the tumor.

The patient was admitted to the hospital in February, 1945, with complaints of lower abdominal pain and vaginal bleeding. Her last menstrual period had occurred in July, 1944, and, having had 15 previous pregnancies, she had assumed herself to be pregnant. She believed she had experienced fetal movements

beginning in October, 1944. Vaginal bleeding for 5 days in November was thought, by her physician, to be evidence of threatened abortion. At the onset of bleeding in February the same physician referred her to the hospital with a presumptive diagnosis of placenta previa.

Examination revealed a semisolid, somewhat mobile mass extending 12 cm. above the symphysis pubis. No fetal heart sounds were audible. The cervix, from which exuded blood, was hypertrophied and exhibited cervicitis and erosion. Anterior and superior to the cervix there was a mobile cystic mass, about 14. cm. in diameter, with a normal sized uterus lying posterior to it. The immediate impression was pedunculated ovarian cystoma with no evidence of pregnancy.

Exploratory laparotomy revealed an extraperitoneal tumor lying anterior to the parietal peritoneum and immediately superior to the apex of the bladder. The mass had a fibrous pedicle superiorly which ran toward the umbilicus, but gradually lost its identity in the surrounding connective tissue. No direct connection existed between the surface of the tumor and the bladder wall. Because of the patient's age and uncertainty as to the cause of uterine bleeding, total hysterectomy and bilateral salpingo-oöphorectomy were performed. Eight months after operation there was no evidence of recurrence of the tumor.

The gross specimen was an encapsulated, irregular mass measuring 15 cm. at its greatest diameter. Sections disclosed large areas of whitish semi-solid gelatinous tumor and cystic spaces. The cavities contained odorless, yellow, slightly mucoid fluid which coagulated on standing. Microscopic sections revealed well-differentiated connective tissue cells, large areas of edema and some hyalinization. The endometrium showed changes typical of menstruation. The tumor was concluded to be a degenerating fibroma of the anterior abdominal wall, with an essentially normal menstruating uterus and multiple ovarian follicular cysts.

While the removed tumor would undoubtedly seem to be a degenerating fibroma, the authors cannot be certain of its urachal origin because the mass had grown to such a size that the normal anatomy of its site was seriously distorted. 1 figure.

(While this tumor by its position might well have been urachal, it is difficult to be sure of this, since fibroma may arise from any of the connective tissues of the abdominal wall. The presence of the tumor, entirely separate from the pelvic organs, could scarcely have had anything to do with the uterine bleeding, which I suppose was most likely of simple functional nature. While tumors of the urachus are very rare, the one most likely to be encountered by the gynecologist is the cyst. Tumors of this cystic type, when large, may lead to difficult diagnostic problems. They are situated in the midline, between the umbilicus and the pubes, and they are ordinarily of ovoid shape. On palpation they give the impression of being attached to the abdominal wall, as indeed they are, since they develop extra-peritoneally, just beneath the anterior parietal peritoneum.—Ed.)

## THE ARTIFICIAL MENOPAUSE AND CANCER OF THE BREAST

L. HALBERSTAEDTER AND A. HOCHMAN

J. A. M. A., 131: 810-816, 1946

Experimental investigations on mice and rats have yielded certain results which are pertinent to the present study. In strains of mice which now show a high percentage of spontaneous mammary carcinoma, early castration of the female reduces the incidence of carcinoma. In strains characterized by a low percentage of spontaneous tumor the administration of estrogen to the female increases the incidence of spontaneous carcinoma. Estrogen administration induces the production of mammary carcinoma in male mice of strains which never develop this tumor spontaneously. Mammary carcinoma can develop in castrate male mice which are implanted with ovaries. Estrogen administration produces mammary carcinoma in rats of a strain which is free from spontaneous mammary carcinoma. The time required for the appearance of mammary cancer depends on the dosage and estrogenic potency of the injection.

Various workers have employed oophorectomy and irradiation of the ovaries in the treatment of cancer of the breast, with results including arrest of the malignant growth and diminution of metastases. However, it is difficult to draw conclusions from the cases reported by various authors because in many cases the metastases and not only the ovaries were irradiated directly. Also, metastases show different degrees of susceptibility to artificial menopause, and some of the cases in which artificial menopause was induced were free from metastases.

In the present paper the authors report their experience with artificial menopause induced in 60 cases; this treatment has proved effective in some and ineffective in others. The 60 patients constituted 15 per cent of a total of 393 women suffering from mammary cancer at the authors' institute. Of the 60 women, 34, or 56 per cent, benefited from the induction of artificial menopause.

Six of the 60 patients had stage I disease (Steinthal's classification), and of these 4 were improved and 2 were not. Twenty-eight patients had stage II disease, and of these 17 were improved and 11 were not. Of 19 patients with stage III disease, 10 were improved and 9 were not. Since the presence of metastases formed the principle indication for treatment, the majority of cases were of stage II and III. From this series it appears that there is no appreciable difference between these 2 groups in regard to proportion of improvement, and it may be expected that the efficacy of interruption of ovarian function, taken as a general measure against metastases, will be independent of the designated stage of the disease.

Irradiation of the ovaries was indicated in most cases which involved metastases of the bone (26 cases). Improvements in this group rated 69 per cent. Metastases of the lung and pleura responded favorably in 50 per cent of cases; cutaneous metastases and local recurrences reacted less favorably; metastases of the lymph nodes showed little response. Brain and liver metastases showed no

beginning in October, 1944. Vaginal bleeding for 5 days in November was thought, by her physician, to be evidence of threatened abortion. At the onset of bleeding in February the same physician referred her to the hospital with a presumptive diagnosis of placenta previa.

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improvement. Of 8 patients showing no clinical evidence of metastases, 6 are well and alive.

On the basis of microscopic observations, there were 18 tumors designated as adenocarcinoma. Improvement was obtained in 13, or 72 per cent, of these cases. Eleven cases were designated as carcinoma simplex, and in this group only one patient reacted favorably to ovarian sterilization. It seems reasonable to conclude that irradiation of the ovaries is especially effective on metastases from adenocarcinoma. The explanation suggested by the authors for this greater vulnerability of adenocarcinoma than carcinoma simplex to withdrawal of estrogenic substance is that histologically the adenocarcinoma tends to reproduce the form of the original alveoli of the gland. This morphological resemblance can be accompanied by a functional resemblance. Therefore, estrogenic substance will be able to stimulate the growth of the adenocarcinomatous cell more readily than it will other varieties of carcinoma cells of the breast, and when this hormone is withdrawn, the malignant adenocarcinomatous growth is deprived of an important growth enhancing factor.

The improvement due to the interruption of estrogenic secretion is of short duration, lasting in the cases in this series with few exceptions from  $\frac{1}{2}$  to 2 years. This is probably due to the fact that ovarian sterilization does not stop completely the flow of estrogenic hormones in the body. Estrogenic hormones can occur in the blood and urine of a woman, even in the absence of periodic bleeding, in both artificial and natural menopause. The origin of the estrogenic substance secreted after castration is still in doubt. In mice, it appears that the adrenals are the site of the vicarious estrogen secretion. The pituitary and the thymus probably share the property of being able to secrete estrogenic substance. Irradiation of the adrenal glands might possibly diminish the estrogen secretion; however, this hypothesis cannot as yet be supported by clinical evidence.

(Oöphorectomy and irradiation of the ovaries appear to have been accepted by many surgeons and radiologists as having a retarding effect upon mammary cancer, especially in the metastatic stage, in women during the reproductive period of life. Unfortunately, a large proportion of such cancers develop in the postmenopausal years, when such treatment would have no rationale. As contrasted with this form of female cancer, stilbestrol therapy seems to have definite virtue in retarding the growth of metastases in prostatic carcinoma. Both these forms of therapy are to be looked upon as palliative, and the careful studies of the authors of this paper would seem to indicate that the results are neither constant nor brilliant in the case of breast cancer. They are inclined to explain the frequent ineffectiveness of the plan by the postmenopausal production of estrogen in the adrenal cortex and possibly other endocrine glands, but quantitatively this is probably a small factor, the more important one being the relentless progress of the disease itself.—Ed.)

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